STRATEGIC R&D ALLIANCES IN TECHNOLOGY INNOVATION BY SMALL BIOSCIENCE FIRMS IN THE U.S.

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Abstract of Dissertation

Strategic R&D Alliances in Technology Innovation by Small Bioscience Firms in the U.S.

The objective of this dissertation research was to examine the impact of strategic research and development (R&D) alliances on biomedical product innovation by small biotechnology firms in the U.S. The following research questions were explored: 1) To what extent can collaborations with different types of partners (e.g., clinical partners, firm partners, university partners) explain product innovation success by small bioscience firms, and 2) How does firm age moderate the impact that different types of partners may have on the firm's innovation success. There were two data sources for this dissertation project: 1) responses from the SBIR Program evaluation survey conducted in 2002 by the NIH, and 2) publications and patent applications by these SBIR grantees. All pertinent scientific papers published and patent applications filed by each SBIR grantee firm between the first year of the SBIR award and 5 years post-award were researched and co-authorship data systematically analyzed in order to identify the firm's R&D collaborators. Inferential statistics to test the influence of different types of partners on innovation success involved logistic regression modeling. The results showed that forming alliances with other firms was more important for start-ups than for older firms. For start-up companies, an increase in the number of corporate partners was both positively and significantly correlated with the firms' innovation success, as measured by successful product development to the commercialization stage. Such relationship did not hold for older firms. Moreover, for the start-up firms, forming R&D alliances with other firms

was more important than forming alliances with universities. An increase in the number of alliances with universities had no statistically significant correlation with an improvement in innovation performance of start-ups nor of older firms. In addition, the inclusion of a large corporate partner had an effect on innovation success that was not observed in the absence of making this distinction in the partner firm attribute in the analysis. Analysis of the role of large corporate partners in the network showed that having a big corporate partner in the alliance network significantly increased the likelihood of innovation success.

Executive Summary

This dissertation research characterized strategic research and development (R&D) alliances and analyzed their impact on biomedical technology and product innovation by small bioscience and biotechnology firms in the U.S. Bioscience and biotechnology broadly encompass the application of science and technology to living systems, and can include applications in diverse areas such as environmental science (e.g., efficient clean up of hazardous waste without the use of caustic chemicals by harnessing the ability of microbes to degrade pollution), animal health, agricultural science (e.g., plant breeding and seeding), and food production and processing. The focus of this dissertation has been limited to bioscience/biotechnology companies that engage in bio**medical** technologies (i.e., therapeutics, diagnostics, and other medical technologies for human subjects), and did not include agricultural, veterinary, or environmental biotechnology. Specifically, firms in three sectors were examined: biotechnology, pharmaceutical, and diagnostics.

Research Questions

The research questions raised to explore the influence of R&D alliances on innovation success by small businesses are as follows: 1) To what extent can collaborations with different types of partners (e.g., firm partners, university partners, clinical partners) explain product innovation success by small bioscience firms; 2) How does firm age moderate the impact that different types of partners may have on the firm's innovation success; and 3) How do R&D network characteristics of small firms differ

among the three bioscience sectors representing biotechnology, pharmaceuticals, and diagnostics. The measure of innovation success was successful product development to the commercialization stage or having the resulting project in use by the target population. The following specific hypotheses were tested in this dissertation: 1) Young firms that engage in (a greater number of) firm-firm collaborations are more successful at innovation than those that do not (i.e., engage only or predominantly in firm-university collaborations); 2) Small bioscience firms (young or old) having ties with large corporate partners are more successful at innovation than those without such ties; and 3) Firms that collaborate with clinical partners are more likely to succeed in the innovation of products subject to FDA regulation than firms that lack clinical partners.

Methods

There were two data sources for this dissertation project: 1) a National Institutes of Health (NIH) survey conducted in 2002 of small businesses that received R&D funding under its Small Business Innovation Research (SBIR) program, and 2) publications and patent applications by these SBIR grantees. The NIH SBIR grantee survey data provided invaluable project level outcome data. Firm level R&D partnership data were collected and compiled by reviewing all pertinent scientific papers published and patent applications filed by each SBIR grantee firm. Scopus by Elsevier was utilized as the primary database accessed for publication and patent search. Once the hit list of publications and patent applications for each firm was generated, the actual papers and patent application documents were retrieved to collect the institutional affiliation information of all co-authors and co-applicants named on the documents. The scientific

content of each document was also reviewed and analyzed in order to be able to characterize the type of collaboration and, by extension, help classify and code the type of collaborator/partner. The firm's R&D partners during the time frame encompassing and flanking the SBIR project period (i.e., starting from the first year of the SBIR award and spanning through 5 years post-award) were identified this way.

The data were subjected to descriptive and inferential statistical analysis using logistic regression models, where innovation outcome served as the dependent variable and different partner types were included as explanatory variables. Information on innovation success was collected from responses to the SBIR survey question, "What is the current status of the project funded by the referenced SBIR award?" The survey responders, who were either the principal investigators or other knowledgeable representatives of the firm, had to select only one of from a list of response choices that included "Under development", "Commercialization stage", "In use by target population", "Discontinued", or "Other."

In addition, various logistic regression models containing interaction terms were used to test the interaction between firm age (i.e., whether it was a start-up or an older firm) and whether or not there was a corporate partner in the alliance network; between firm age and whether or not there was an academic partner in the alliance network; between FDA regulation (i.e., whether or not the product required FDA approval) and whether or not there was a clinical partner in the alliance network. The classification of partner types into corporate or academic was based on the practice established by prior alliance research on the benefits as well as the costs of R&D collaborations and their influence on firm success, in which various authors focused on the role of corporate

partners or the influence of academic partners. For this dissertation research, clinical partners such as hospitals and medical centers were included as another partner type. Start-ups or "young firms", as referenced in the first hypothesis, were defined as firms less than 4 years old. Big firms or "large corporate partners", as referenced in the second hypothesis, were defined as firms with over 1000 employees.

Summary of Findings

Descriptive analysis of partnership characteristics showed that the behavior of biotechnology and pharmaceutical firms with respect to the number of linkages they formed with different types of partners was similar and comparable. Both biotechnology and pharmaceutical firms had the greatest number of linkages with basic/academic research institutions (i.e., universities, federal laboratories, and non-profit research institutes) over the other types of partners, with greater than 75% of biotechnology and pharmaceutical firms having one or more linkages with academic or basic research institutions. Diagnostics firms were by far the least likely to engage in R&D collaborations with other firms. Almost 50% of diagnostics firms had no linkages with other firms. Analysis of interfirm linkages showed that biotechnology firms tended to form alliances with other biotechnology firms, while pharmaceutical firms tended to form alliances with other pharmaceutical firms. However, CROs and service providers comprised the greatest proportion of firms with which the diagnostics firms formed R&D partnerships. In fact, one-third of the linkages formed by the SBIR diagnostics firms were with CROs and service providers.

The results from inferential statistics showed that for start-up companies, having a

corporate partner in the alliance network was associated with over 6-fold increase in the odds of innovation success, but having an academic or a clinical partner was not associated with a change in the odds of innovation success. Moreover, start-up firms having a greater number of alliances with other firms were more likely to successfully innovate, where the odds of innovation success increased by approximately 77% for every additional interfirm alliance. For start-up firms, forming R&D alliances with other firms was more important for innovation success than forming alliances with universities. Such relationship did not hold for older firms. For the older firms, having a corporate partner in the alliance network was not associated with statistically significant change in the odds of innovation success. From this it was concluded that forming alliances with other firms was more important for start-ups than for older firms. As was observed for start-up firms, alliances with academic partners or clinical partners were not associated with improved innovation performance by older firms. For the SBIR small businesses, without distinguishing whether they were start-ups or older firms, having a large corporate partner in the alliance network was associated with over 2-fold increase in the odds of innovation success.

As expected, the need to obtain FDA approval was a strong predictor of decreased innovation success. As compared to a product that did not require FDA approval, the odds of success in innovating an FDA-regulated product were approximately 88% lower. Alliances with clinical partners, however, did not help increase the likelihood of innovation success of products subject to FDA regulation. One explanation for this is that classification of clinical partners may not have been sufficiently rigorous to distinguish them from the academic partners, as many hospital and medical center scientists are

jointly affiliated with universities and conduct basic rather than clinical research.

Policy Implications

Recommendations based on the above findings are that public policy aimed at fostering innovation should give attention to helping start-up companies engage in R&D collaborations with other firms, and helping small businesses forge R&D alliances with big firms. Informed by the finding that bringing together certain types of partners for collaborative R&D can increase success in innovation by small businesses, policies of agencies that support biomedical R&D could incorporate conditions for public funding that incentivize such interactions in the expansion of its existing programs and the design of new initiatives.

It would be possible to promote the participation of big firms in interfirm collaborations by providing financial incentives established through public funding or cost-sharing by the government when a large firm undertakes an R&D project jointly with a small firm partner. Similarly, initiatives with the objective of assisting start-ups attract corporate partners could be crafted with language in the eligibility criteria that require, for instance, the lead partner in a joint venture that applies for government funding to be a start-up firm. This could promote their desirability as partners to other firms.

From an economics standpoint, one of the main rationales for government support of R&D programs is to remedy market failure. Market failure arises because a firm is not going to invest in R&D if it cannot capture a significant portion of the social benefits from the new knowledge, technology, or product generated by the R&D. According to

economists who had evaluated the SBIR and other similar programs, R&D subsidy programs should seek to maximize the social rate of return and select projects for funding based on whether they would generate large spillovers (i.e., social benefits that are not captured by the firm conducting the R&D). We need to also recognize that social returns and spillovers cannot be realized without successful commercialization of the new technology or the new discovery because market spillovers are entirely dependent on commercialization and knowledge spillovers are also greatly dependent on commercialization. With expected social returns from innovation being a function of the magnitude of social returns from innovation and the probability of success in innovation, the findings of this dissertation could help R&D subsidy policies and programs maximize expected social returns by increasing the probability of innovation success. Lastly, policies that integrate the recommendations of this dissertation may not impact non-bioscience sectors is the same way that it influences bioscience sectors. The results would be generalizable to the extent that the sectoral and national innovation systems are comparable to that of the pharmaceutical and biotechnology sector (e.g., the agents through which the path of knowledge flow and accumulation are comparable, the distribution and diffusion of competencies are comparable, and the types and nature of vertical and horizontal relationships among the various agents are comparable).

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CHAPTER 1: INTRODUCTION

The objective of this dissertation research was to examine the impact of strategic research and development (R&D) alliances and partnerships on biomedical product innovation by small bioscience and biotechnology firms in the U.S. Collaborative R&D is considered a "strategic" partnership when strategic logic forms the basis for a firm's rationale in undertaking that activity to achieve its profit maximizing objective. An underlying strategic logic shapes the kinds of management processes the firm uses to identify and acquire various tangible and intangible resources in pursuit of competitive advantage (Sanchez & Heene, 1997). While Standing et al. have defined "strategic alliances" as "cooperative agreements between firms that create value for participants by providing competitive advantages and synergies" (Standing et al, 2008), strategic alliances are not limited to just firms. Research partnerships inclusive of universities, non-profits organizations, and government laboratories may also be referred to as strategic alliances. These partnerships can be administered through many different types of arrangements (e.g., R&D contracts; joint R&D agreements; cooperative agreements; research joint ventures; licensing), but this dissertation did not distinguish the specific mechanism by which the partnerships were formed.

Bioscience and biotechnology broadly encompass the application of science and technology to living systems, and can include applications in diverse areas such as environmental science (e.g., efficient clean up of hazardous waste without the use of caustic chemicals by harnessing the ability of microbes to degrade pollution), animal health, agricultural science (e.g., plant breeding and seeding), and food production and processing. The focus of this dissertation has been limited to bioscience/biotechnology

companies that engage in bio**medical** technologies (i.e., therapeutics, diagnostics, and other medical technologies for human subjects), and did not include agricultural, veterinary, or environmental biotechnology.

In the academic fields of Management Science, Business Administration, and Science and Technology (S&T) Policy, the term "innovation" means "bringing to market." This dissertation research began by pondering what factors could influence innovation success particularly by small businesses. Under what organizational arrangements or conditions are discoveries turned into marketable products while in other cases they just fade away? The following are the dissertation research questions raised to explore the role that R&D partners may have on innovation success: 1) To what extent can collaborations with different types of partners (e.g., clinical partners, firm partners, university partners) explain product innovation success by small bioscience firms, and 2) How does firm age (representing firm maturity or stage of firm development) moderate the impact that different types of partners may have on the firm's innovation success.

These research questions generated the following specific hypotheses: 1) Young firms that engage in greater number of interfirm collaborations are more successful at product/process innovation than those that have very few interfirm collaborations and engage predominantly in firm-university collaborations; 2) Bioscience firms having ties with large corporate partners in their alliance network are more successful at product/process innovation than those that do not have such ties; and 3) Firms that collaborate with clinical partners are more likely to succeed in the innovation of products subject to the FDA (U.S. Food and Drug Administration) regulations than firms that lack clinical partners.

Firms in three sectors were examined: biotechnology, pharmaceutical, and diagnostics. A special focus has been placed on analyzing the partnering behavior of diagnostics companies and examining the types of firms with which they actively collaborate. Despite the pervasiveness of biotechnology adoption and application by diagnostic firms, there is a lack of studies involving firms in this category. Moreover, diagnostics can have critical importance in the development of drugs (e.g., for patient selection or stratification in clinical trials), and has a central role in the concept of personalized medicine that is becoming increasingly popularized.

This dissertation research contributes to and extends the **alliance/partnership literature** by adding **empirical data** to the theoretical concept of complementary partnerships in the resource-based view of the firm, and by testing the importance of specific partner types for small, bioscience firms. Specifically, **project level** performance data of a large number of firms in the biotechnology industry have never been systematically analyzed before and conducting such analysis is a unique value added feature of this dissertation research.

Another way that this dissertation research helps expand the literature is by examining **innovation as a measure of performance**, since most other alliance research has focused predominantly on financial/economic or market performance. With translation (i.e., taking basic research discoveries into the clinic) as the goal program initiatives by public health mission agencies like the NIH, "innovation" defined as bringing new products to market is fitting as the target performance measure. Market performance, on the other hand, bears on firm growth, which is beyond the interests and objectives of NIH. That is, NIH's concerns would be on whether the products become

available for public health benefit rather than whether the firms achieve financial success. Innovation may lead to market success for firms, but how well the products perform in the market in the long run would entail studying variables that are beyond the R&D level.

This dissertation contributes to the **strategic management literature** in that the insights generated regarding the types of partnerships that could lead to greater innovation success may guide corporate networking strategies, vis-à-vis partner selection for a more successful outcome. While most prior alliance research has focused on either firm partners or university partners and their respective influences independent of the other, this dissertation research has examined both types of partners in a comparative mode. From a policy perspective, the insights generated by this dissertation research into how variations in partnering could influence small bioscience firms' performance in innovation may help identify the types of collaborative interactions to foster. The ultimate goal is to inform science and technology (S&T) and innovation policies aimed at enabling strategic R&D partnerships to facilitate the innovation of biomedical technologies.

The remainder of this dissertation is organized as follows. Chapter 2 provides background on the evolving interactive dynamics between the pharmaceutical and biotechnology industries to set the stage for how these biopharmaceutical industries operate. Details on the types of products generated by bioscience firms and what is involved in their R&D process should enable the readers to understand the unique needs of bioscience firms and why the focus on certain partner types would be appropriate. Chapter 3 on the theoretical framework includes a review of existing theories on firm behavior and the actions that firms take to enhance performance and competitiveness.

These theories help lay the foundation for rationalizing the types of partners that could positively influence firm success in innovation. Chapter 4 provides a literature review of studies that have focused specifically on factors that characterize effective partnerships and have asked questions that are similar to those asked in this dissertation. Chapter 5 delineates the research questions and hypotheses tested in this dissertation, and Chapter 6 describes the data sources, the variables, quantitative methods, and the statistical models used to test the hypotheses. Chapter 7 presents the data and the results of statistical analyses and, finally, Chapter 8 not only provides a discussion around the results and new insights generated for scholars and business managers, but also includes an extensive section on the policy implications and prescriptions.

CHAPTER 2: BACKGROUND

Evolution of Interaction Between Biotechnology and Pharmaceutical Industries

The dynamics of interfirm R&D relationships we observe today in the biopharmaceutical industry, including the way partnerships and licensing agreements are forged between the start-up or small bioscience firms and the large pharmaceutical or large biotechnology firms, have been shaped by evolving organizational structures and business models of the biotechnology and pharmaceutical industries. This section provides some insight into how economic forces have given rise to specialization in the biotechnology industry, leading to submarkets representing distinct R&D trajectories. At the same time, there has been a blurring of the demarcation between the pharmaceutical industry and the biotechnology industry, leading to the biopharmaceuticals market. With an understanding of this landscape, we can better appreciate the strategic behavior of the firms belonging to these industries and the importance of forging relationships with certain types of R&D partners.

A few pioneering biotechnology companies founded in the mid-1970s and early-1980s, such as Genentech and Amgen, were successful in establishing an organizational structure modeled after the *fully integrated pharmaceutical company*, where the processes of discovery, development, sponsoring of clinical trials, manufacturing, distribution, and sales were all carried out within the company. Their business model was guided by a vertically integrated strategy of controlling all processes from drug discovery to marketing and sales. However, the biotechnology industry as a whole failed to make

this strategy work for three reasons: limited capital, lack of management know-how, and distance from the public consumer market (Scarlett, 1999).

First, there was an overwhelming need for large amounts of *capital*, but the rapidly increasing number of new companies that entered the biotechnology industry resulted in a fierce competition for investor capital and the limited financing available. This is what Carroll and Hannan described as resource scarcity and niche crowding that result from competition forces and increase the risk of failure for start-ups (Carroll & Hannan, 1989). Most biotechnology companies faced a financial crunch in an overburdened capital market. The *lack of management know-how* was due to the fact that the scientist-entrepreneurs were not suitably qualified to run a biotechnology company. Moreover, it was nearly impossible to find in a single manager someone who understood the *entire* process of moving a product from discovery through development and on to the market because the most likely place to get such training — the pharmaceutical companies — had segmented the entire process into different divisions. Most of biotechnology's management tended to come from the scientific discovery end, i.e., the front end of business, which was fine for the administration of basic science R&D endeavors; but this became a real problem for the companies when confronted with the need to move products successfully through the downstream value chain activities and later stages of commercialization. Finally, there was biotech's *consumer market* problem. The biotechnology industry was far removed from the consumer market for drugs and therapeutics, which existed completely within the purview of the pharmaceutical industry.

Hence, biotechnology companies licensed their most promising products to big pharma and received upfront cash payments, as well as follow-on R&D and milestone payments associated with the technology or product being licensed. The biotechnology companies would eventually accrue royalty income on commercialized products, but the royalty was usually a single digit percentage of net sales. The cash-strapped biotechnology companies accepted these deals because the upfront cash and continued R&D support kept their research going and, also, the prestige of having a pharmaceutical partner(s) enhanced their credibility in the financial markets. However, biotechnology companies could not make money through this route, especially since the upfront fees were small relative to the implicit value of the innovations shared or given up, and the bulk of the milestone payments were at a discounted rate because of the huge "risk" the pharmaceutical companies were assuming. The real financial benefits went to the big pharma partner, and many biotechnology companies became marginalized drug discovery and development assets of their pharmaceutical partners.

Nonetheless, licensing continues to be an integral component of the biotechnology industry's business model, especially since the costs associated with later development involving phase III clinical trials have traditionally been and still are beyond the means of small biotechnology companies that do not already have products yielding substantial revenue. Thus, most biotechnology companies have little choice but to turn to the pharmaceutical industry for the development of their products after investigative new drug (IND) filing with the FDA and phase I and II clinical studies. In the process, biotechnology companies gain some access to regulatory expertise and learn how to build manufacturing and marketing capabilities.

The pharmaceutical industry, for its part, entered into relationships with the biotechnology industry out of necessity as well. As a mature industry, the pharmaceutical industry was no longer able to innovate at a rate that justified the premium drug pricing it had enjoyed. Pharma needed to develop innovative products, and it recognized that biotechnology could provide the way to innovation. Start-up biotechnology companies were developing state-of-the-art platform technologies capable of generating greater numbers of lead compounds, as well as drug and drug target candidates for development, than was possible using pharma's traditional methods involving organic medicinal chemistry and screening.

During the early years of the biotechnology boom, big pharma moved into this sector by outright acquiring these biotechnology companies. Since buying biotechnology platform companies while only using a fraction of their capabilities was expensive and wasteful, pharma's strategy changed to that of acquiring or licensing specific technologies or products that were well advanced in their development phase. The pharmaceutical partner would then assume the responsibility for clinical development and commercialization.

In general, pharmaceutical companies have a well-established business model for managing the commercialization phase involving regulatory processes, marketing, distribution, and reimbursement. The early-stage discovery R&D phase of drug development, on the other hand, is increasingly being contracted out and outsourced. An example of pharma giant that views and manages R&D functions as noncore is GlaxoSmithKline (GSK, UK), which reorganized its R&D units several years ago and launched a hub-and-spokes model, where the R&D units are independently organized

around a core hub containing phase III clinical trial management capabilities, marketing, manufacturing and corporate functions (Mehta, 2004). The investment that pharmaceutical companies make in biotechnology companies through collaborations and alliances accounts for a significant portion of this nation's R&D spending in biosciences.

In order to meet such demands of the pharmaceutical industry, the biotechnology industry has spawned a new generation of highly specialized biotechnology companies, whose business model is to focus on those aspects of the drug development process where their expertise added real value. What emerged are the discovery and research tool companies. These companies focus exclusively on platform technologies enabling the identification of new drug targets and potential therapeutic leads. They sell to the pharmaceutical companies the tools to do this discovery on their own or the services to do the work for them. Affymetrix and Millenium are examples of tool companies whose R&D-related income, rather than a drug product, is the principal driver of earnings. Instead of the fully integrated pharmaceutical company model, these biotechnology companies have patterned themselves after other high-technology companies that are paid for developing highly specific capabilities (Scarlett, 1999). Such biotechnology companies do not need to have toxicologists, regulatory affairs professionals, or pharmaceutical marketers within the organization. Competitiveness within discovery tool companies is defined by success in achieving improvement and innovation within their defining technologies. The challenge for them is in keeping up with multiple latest technologies that could become the new components to be integrated into or replace their existing platforms, and this would require their collaboration with other high technology (e.g., nanotechnology) companies.

Another group of bioscience companies, whose numbers are increasing, is comprised of contract research organizations and clinical research organizations (CROs). These companies specialize in preclinical toxicology, regulatory and clinical trial capabilities, and process development; and they do not incur the fixed R&D costs associated with a discovery-based biotechnology company. Since the mid-1990s, CROs have become a large presence at industry meetings, and now there are conferences devoted entirely to industry-CRO relationships, the largest being the Partnerships with CROs conference held annually and supported by the Institute for International Research (http://www.iirusa.com/cropartners/eventhome.xml). Bioscience companies are now routinely turning to CROs for services that include drug formulation and synthesis; clinical trial management (e.g., design of protocols, monitoring of trials); laboratory services (e.g., sequencing, in vitro testing, central processing of tissue resources); and preparation of documents for submission to the Food and Drug Administration (e.g., New Drug Application, Abbreviated New Drug Application).

Biopharmaceutical Market

There are differing perspectives on just how successful small biotechnology entrants have been in breaking into the human therapeutics market by commercializing their new technologies, and how well large pharmaceutical companies have adopted biotechnology to maintain their dominance. Moore claimed that small companies would "win more often in the large-molecule 'biologicals' sector of the market" where they are able to make fast progress, and increasing affordability of molecular biology and screening technologies has considerably narrowed the gap between the type of research

done in large and small companies (Moore, 2003). On the other hand, Teece saw fully-integrated pharma incumbents as best positioned to benefit from radical technological change through exploitation of the firms' existing complementary assets (Teece, 1986). Complementary assets here refer to the non-technological, market-related assets such as regulatory, manufacturing, marketing, and distribution expertise and access necessary to successfully commercialize a new technology or product.

While biotechnology has created a new industry and a new market for biodrugs, it stopped short of being a "disruptive" technology as it did not eliminate or displace the existing pharmaceutical market or its traditional drug discovery technology that is chemistry-based and involves high-throughput screening. In fact, biotechnology has been called a "sustaining" technology that has enabled incumbent pharma to sustain its trajectory of performance improvement and stay on top (Christensen, 1997).

Pharmaceutical companies have indeed been extremely successful in adopting biotechnology, with a subset of their product profiles overlapping those of the biotechnology firms. With protein therapies having a market value in excess of $57 billion in 2006 and a growth rate of 12 percent until year 2010 (RNCOS, 2007), big pharma saw the blockbuster potential of this area and has been penetrating the protein therapeutics market of the biotechnology industry. Incumbents pharmaceutical companies leveraged their complementary assets by collaborating with new biotechnology firms, and used these interfirm collaborations as *a mechanism for adapting* to radical technological change (Rothaermel, 2001).

Meanwhile, many new biotechnology companies continue to enter this market, making the nexus of partnerships and licensing agreements between big pharma and

biotech, as well as among the biotechnology companies big and small, more dense. What is observed nowadays is that the biotechnology and pharmaceutical industries are becoming increasingly intertwined. As Rothaermel phrased it, there is a "a symbiotic coexistence between incumbent firms and new entrants in the biopharmaceutical industry following radical technological change" (Rothaermel, 2001). Many biotechnology companies developing biodrugs are now referring to themselves as "biopharmaceutical" companies and even incorporating the term "pharmaceutical" into the company name, making the job of distinguishing them from the traditional pharmaceutical companies challenging for scholars. **Table 1** lists some of the most promising biopharmaceutical products being developed for cancer therapy, and it illustrates the integration of these two industries in the development and distribution of these products.

Table 1. Biodrugs for cancer currently in development or on the market.

Drug	Trade Name	Description (and Mechanism)	Disease	Developer
Alemtuzumab	Campath or Campath-1H	Recombinant DNA-derived humanized monoclonal antibody against CD52, glycoprotein present on surface of mature lymphocytes	Chronic lymphocytic leukemia (CLL), T-cell lymphoma	Developed by **Genzyme (biotech)**; distributed by **Bayer (pharma)**
Bevacizumab	Avastin	Monoclonal antibody against vascular endothelial growth factor (VEGF); inhibits angiogenesis (formation of new blood vessels)	Colorectal cancer, non-small cell lung cancer; renal cell carcinoma, breast cancer, among others	Developed by **Genentech (biotech)**; distributed by **Genetech** in US and by **Roche** (Genetech's parent **pharma** company) elsewhere
Cetuximab	Erbitux	Chimeric monoclonal antibody inhibitor of epidermal growth factor receptor (EGFR)	Colorectal cancer, head and neck cancer, lung cancer	Developed by **ImClone (biotech)**; distributed by ImClone and **Bristol-Myers Squibb (pharma)** in North America and by **Merck (pharma)** elsewhere
Gardasil	Gardasil	Vaccine comprised of human papilloma virus (HPV) major capsid protein L1 that can spontaneously self-assemble into virus-like particles (VLPs); contains recombinant VLPs assembled from L1 proteins of HPV type 6, 11, 16 and 18.	Cervical cancer	Developed by the US **National Cancer Institute (government)**; licensed and distributed by **Merck**

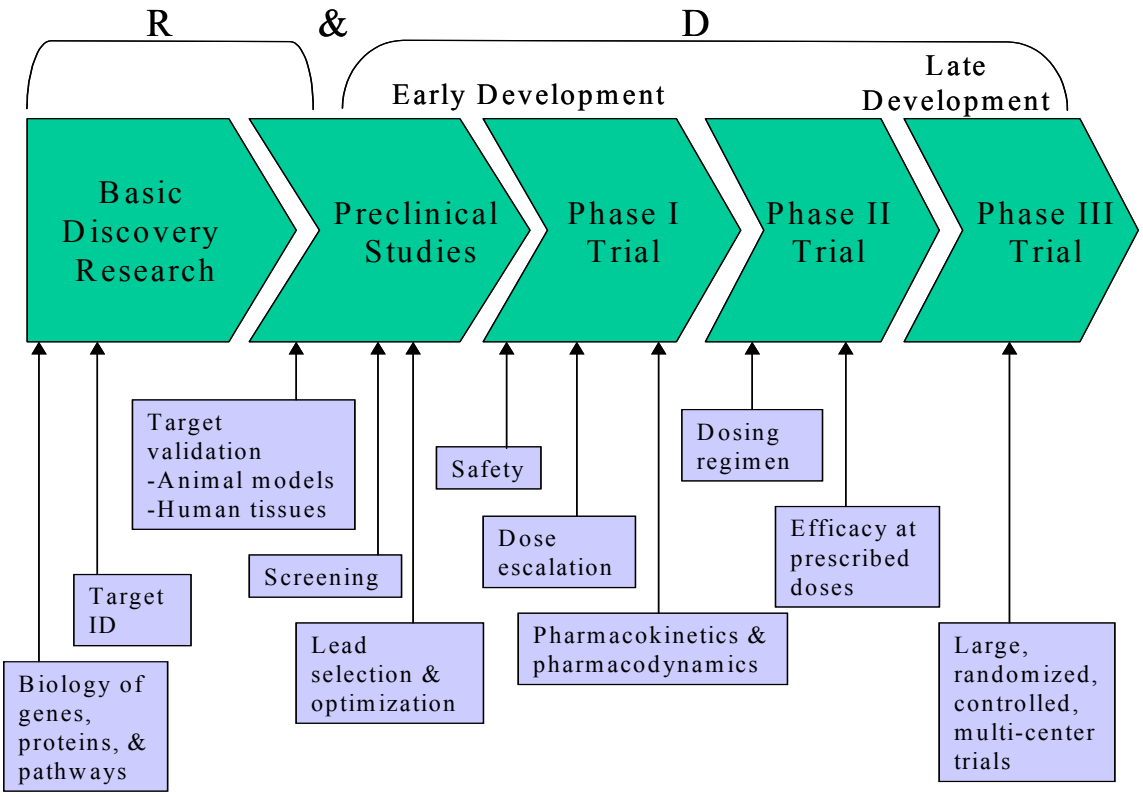
Table 1. Biodrugs for cancer currently in development or on the market (continued).

Drug	Trade Name	Description (and Mechanism)	Disease	Developer
Panitumumab	Vectibix	Monoclonal antibody (IgG2) inhibitor of EGFR	colorectal cancer (for patients expressing EGFR; only effective in patients having wild type KRAS gene)	Developed by **Amgen** (**biotech**)
Pertuzumab	Omnitarg	Monoclonal antibody inhibitor of HER dimerization. Works by binding to HER2 and inhibiting its dimerization with other HER receptors.	prostate, breast, and ovarian cancers	Currently being developed by **Genentech**
Rituximab	Rituxan	Chimeric monoclonal antibody against cluster of differentiation 20 (CD20) widely expressed on B-cells; depletes B-cells	B cell non-Hodgkin's lymphoma (NHL)	Developed by **IDEC Pharmaceuticals (biotech)**; distributed by **Biogen Idec (biotech** formed by merging of Biogen and IDEC**)** and **Genentech** in US and by **Roche** in EU
Trastuzumab	Herceptin	Monoclonal antibody that binds to and inhibits HER2/neu (erbB2) receptor (tyrosine kinase); induces cells to undergo G1 arrest	Breast cancer (for patients expressing HER2/neu receptor)	Developed by **Genetech**
TroVax	TroVax	Vaccine delivering tumor-associated antigen, 5T4, using a pox virus vector	Most solid tumors -- renal cell carcinoma, colorectal cancer, prostate cancer, among others (expressing 5T4 tumor antigen)	Being developed by **Oxford BioMedica (biotech)** and **Sanofi-Aventis (pharma)**

Stages of R&D in Bioscience

In this section, the stages of R&D process for biomedical products and what is meant by research versus development are explained (see Figure 1 below). Clarifying the unique needs and challenges for research versus development will help provide additional context for us to better understand the implications of differentiating the partner types into the groups specified in this dissertation's hypotheses. It is particularly important to better define the term "development," as there appears to be some disconnect between how this term is used by the practitioners within the industry versus the scholars and academics who study the industry from the outside and generate theories about firm behavior. For example, in his examination of the impact of strategic alliances in the "biopharmaceutical industry," Rothaermel classified alliances into two groups: exploitation alliances and exploration alliances. He coded "technology-oriented alliances that focus on drug discovery and development, as well as clinical and commercial manufacturing" as exploration alliances, while "market-oriented alliances that focus on clinical trials, FDA regulatory management, and marketing and sales" were coded as exploitation alliances (Rothaermel, 2001). What is problematic here is that clinical trials are, in fact, at the center of drug development in biotechnology and pharmaceutical industries, but the way "development" and "clinical trials" have been grouped separately indicates that the author may not have grasped this concept. This background section will help inform the reader of usage of R&D terminology, as it applies to the biotechnology and pharmaceutical industries.

Figure 1. Research and development continuum in biomedicine.



Research

Research in biomedicine is carried out for the most part at the laboratory bench and involves working with *in vitro*, *in vivo,* or *in silico* model systems to conduct primarily hypothesis-driven studies of the working of biology and disease processes. Cumulative knowledge generated from such research lays the foundation for biomedical discoveries. The traditional means of drug discovery in the pharmaceutical industry has long involved less hypothesis-driven and more high-throughput screening type of

research, although the current prevalence of molecular biology in almost every aspect of biomedical research and the increasing application of genomic and proteomic methodologies have effected changes in search strategies for drugs and biodrugs.

This discovery step is followed by preclinical testing. Preclinical testing, usually performed in animal models, can be considered part of the *research* phase of R&D if it generates mechanistic insight; or the *development* phase if the goal is principally to determine the pharmacokinetics, pharmacodynamics, and toxicity, and is performed following good laboratory processes (GLPs) as specified in the regulations of the FDA. For in vitro diagnostics, such preclinical testing would involve assay validations, and could be considered either research or development.

Development

Once preclinical testing and validation have been completed, a sponsoring company or institution conducts clinical trials. This is the *development phase* of R&D, and new products designed for use in humans are required by law to be tested in clinical trials before they can be marketed (although there are some exceptions in diagnostics). Following approval by an institutional review board, the sponsor files an investigational new drug application (IND) with the FDA for authorization to test their drug in people. These IND applications go to FDA's Center for Drug Evaluation and Research (CDER) if the product is a therapeutic protein, peptide, or small molecule synthetic drug. They go to the Center for Biologics Evaluation and Research (CBER) if the product is a vaccine, gene- or cell-based therapy, or blood product. Diagnostics and devices undergo a different set of regulatory processes.

Clinical trials are usually comprised of three phases, and those working in the biotechnology and pharmaceutical industries frequently **indicate different stages of product development by referring to the phase of clinical trial – e.g., "phase II development" or "phase III development."** A product in the phase I trial stage is considered to be in "early development." A phase I clinical trial for determining the safety and toxicity of a therapeutic agent can take as little as 6 months from start to finish and include 10-100 trial volunteers at a cost of about $10 million; a phase II trial to determine the efficacy, as well as the dosing and schedule information, usually tests 50-500 people over the course of 12-24 months at a total cost of more than $20 million; and a phase III trial performed to confirm the efficacy in a large patient group involves several hundred to several thousand study participants and may take 3-5 years at a cost of $80-$100 million (Rosin & Scott, 2006). Once the product has been demonstrated to be effective in clinical trials that were performed under good clinical practice (GCP) guidelines, which provide assurance that these studies are credible and that the rights of all human subjects have been protected, it is then submitted for marketing approval. Most drugs, unfortunately, fail at some point during development because of toxicity or immunogenicity, or just do not work in humans as they did in animal models.

After GLP, GCP, and good manufacturing practice (GMP) regulations have been followed and the product has performed successfully in a phase III clinical trial, the sponsor files a new drug application (NDA) or biologics license application (BLA) with the FDA. If this product application gets approved, the sponsor has a license to market the product. Overall, product development timelines from discovery to market launch can range from 7 to 11 years for traditional pharmaceuticals and 4 to 8 years for biomedicines

(Powell, 1996).

Innovating new diagnostics may also face regulatory challenges, since the commercialization of new in vitro diagnostic (IVD) assays must undergo FDA clearance. There are two primary routes by which new IVD assays can enter the market in the United States: through the submission of a **510(k) premarket notification** or the lengthier and more costly **premarket approval application (PMA)**. In order for a 510(k), which is available to low to moderate risk Class I and Class II devices, to be cleared by the FDA, the new IVD needs to be substantially equivalent to a "predicate device." A predicate device is another assay that has been previously cleared by the FDA. 510(k) applications must be supported by clinical data.

New Class III (i.e., high risk) devices must obtain PMA approval, which requires demonstrating that the product is safe and effective for intended use. For example, cancer screening assays are generally placed in Class III. Obtaining approval for PMA requires more data from clinical studies than for a 510(k). A biomarker for screening requires data from a large, prospective study, while a small, retrospective study could be adequate for a monitoring biomarker. An IVD can also be placed in Class III if there is no predicate device. For example, when a company submits a 510(k) for a novel, low risk protein-based assay but is unable to identify an acceptable predicate device, the product is automatically placed in Class III. However, FDA has the latitude to "de novo" reclassify the device to Class II and essentially treat the submission as a 510(k), which can greatly shorten the time to market. Historically, laboratory-developed tests have not been regulated by the FDA. Instead, these tests are regulated by the Centers for Medicare and Medicaid Services under the Clinical Laboratory Improvement Amendments passed by

the Congress in 1988. Overall, obtaining FDA clearance or approval for most novel IVDs is not simple or routine, and requires thorough planning of a regulatory strategy.

As described, the process of developing new drugs, biodrugs, and sometimes diagnostics is not only research-intensive and extraordinarily costly, but the regulatory hurdles surrounding mandatory clinical trials add a layer of complexity to the development of products in the biotechnology/bioscience sector that does not exist in other high technology industries. Awareness of these clinical aspects of the development process for many biomedical products should help us recognize and appreciate the significance of identifying and studying the impact of clinical partners in R&D alliances.

Small Business Innovation Research (SBIR) Program

The data for this dissertation research came from the grantees of the Small Business Innovation Research (SBIR) program, which was established in 1982 under the Small Business Innovation Development Act (PL 97-219). The Program was reauthorized in 1992 (P.L. 102-564) and again in 2000 (P.L. 106-554). The most recent reauthorization will set to occur in 2010.The statutory objective of the SBIR program is to strengthen the role of innovative small businesses in federally-funded R&D. As specified in the Act, SBIR program goals are to 1) stimulate technological innovation, 2) use small business to meet federal R&D needs, 3) foster and encourage participation by socially and economically disadvantaged small businesses and by small businesses that are majority owned and controlled by women, and 4) increase private sector commercialization of innovations derived from federal R&D, thereby increasing competition, productivity, and economic growth.

Under the SBIR Program, federal agencies with an R&D budget over $100 million must set aside 2.5% of their budget for grants to small businesses. The SBIR program consists of three phases. In Phase 1, the agency may award up to $100,000 for a period not to exceed 6 months for a firm to work on demonstrating the scientific and technical feasibility and commercial merit of their proposed research idea or project. In Phase 2, the agency may award up to $750,000 for a period not to exceed 2 years for the firm to further develop the R&D projects initiated in Phase I. In Phase 3, the firm receives no SBIR funding but is expected to commercialize the resulting product.

In determining whether a business qualifies for **small business status**, the Small Business Administration (SBA) considers **the size and ownership** of the business and all of its affiliates. In this regard, the affiliates include companies that have license or merger agreements, firms that are economically dependent based on contractual relationships (identity of interest), joint ventures, and new businesses that fall under the "newly organized concern rule" [i.e., new businesses that have been organized by former key employees (or officers, directors, managing members, principal stockholders) of another business in the same or related industry and in which they serve as key employees (or officers, directors, principal stockholders, and managing members) of the new business, and one business is furnishing the other with contracts, facilities, financial assistance or technical assistance]. The small business entity must be "independently owned and operated" (i.e., have at least 51% ownership and control by one or more natural persons of the U.S., or by another business concern that is itself majority owned by natural persons of the U.S.) and meet the small business size standard of having 500 or fewer employees working at the business and its affiliates defined above.

CHAPTER 3

THEORETICAL FRAMEWORK

This chapter contains a review of the literature on diverse theories that formed the basis for the hypotheses that have been generated and tested in this dissertation. As this dissertation is focused on strategic partnerships and alliances, various theories on why alliances are formed (the causes) and what benefits they provide (the consequences) have been examined. The following chapter will then review various empirical studies on alliances. Theories that have contributed over the years to the analyses of alliance formation include the resource-based view, competence-based view, knowledge-based view, and dynamic capabilities theory. All of these inter-related theories are various perspectives of the strategic management theory, which provided the foundation for this dissertation's theoretical framework.

The **strategic management theory** tries to explain **firm performance** through various concepts under "strategy" relating to business processes at the firm level, such as competitive advantage, core competencies, and resource-based management. While firm "performance" in the strategic management theory generally refers to financial performance and to profits in particular, this theory can nonetheless provide the framework for explaining R&D performance and innovation success as well. The strategic management field analyzes firm performance in a comprehensive manner as a function of a firm's distinctive competencies and industry-specific attributes. It deals with how **industry characteristics** and **firm competencies** relate to each other to shape or sustain a firm's competitive advantage. Different perspectives or "views" that comprise

the strategic management theory are discussed in more detail throughout the remainder of this chapter.

SWOT analysis is an example of a perspective that has not only improved our understanding of strategic management but has actually been of use for practitioners (Priem & Butler, 2001). It is a method of exploring possible strategic alternatives by evaluating a combination of strengths (S), weaknesses (W), opportunities (O), and threats (T) involved in a project or business venture. The strengths and weaknesses refer to those internal to the firm, while opportunities and threats refer to those found in the external, competitive environment. Examples of strengths could include a strong management team and great location. Weaknesses could include insufficient cash resources and weak sales expertise. A price sensitive market, economic slowdown, and entrance of a major competitor into the market segment are all examples of threats. Finally, a market that is poised for growth, potential export markets, and new distribution channels could constitute opportunities. SWOT analysis results are considered in strategic decision-making, together with other internal and external factors that would be favorable or unfavorable toward achieving the objectives of the business venture. Hence, consideration of alliances, whether done intuitively or in a more systematic manner, could be included in this type of analysis.

The strategic management theory also views the firm as an open system of asset and resource flows, and as a dynamic learning organization that can build competencies through the integration of external resources and knowledge derived from alliances and networks. This aspect of the theory focuses on the mechanisms by which firms access new resources and knowledge and deploy new skills.

Resource-Based View

As previously mentioned, there are several perspectives within the field of strategic management that tend to be better suited toward addressing certain issues over others. One important perspective is the resource-based "view" for analyzing the sources of competitive advantage. The resource-based view argues that a firm's performance depends on its ability to have sustainable competitive advantage derived from possessing or having control over unique resources (i.e., unique human, organizational, and material resources and skills) (Barney, 1991; Rindova & Fombrun, 1999). It emphasizes the accumulation and control of resources within the firm and explains the differences in the performance of firms in terms of their different resource endowments.

Elements of the resource-based view can be found in the work by Edith Penrose on her theory of the growth of the firm, although the "resource-based view" as it is recognized today was not adopted within the field of strategic management until the 1980's with the seminal article by Wernerfelt entitled, "A Resource-Based View of the Firm" (Priem & Butler, 2001; Wernerfelt, 1984). Penrose noted that as a firm grows and achieves a reasonably secure position in its original business, it can generate resources in excess of what is required for maintaining that position and may look to opportunities for diversification (Penrose, 1959). While Penrose emphasized the role of resources in diversification and leveraging of resource-based advantages for the firm's expansion into new products and markets, the resource-based view generally attempts to explain the contribution of resources to the advantages of one growing firm over another in terms of how a growing firm achieves its initial, secure position in a particular product market

(Priem & Butler, 2001).

Wernerfelt's article is considered extremely significant because it redirected strategy scholars' attention to looking at firm assets and resources rather than at the product market as the source of firm's competitive position and of entry strategies for firm diversification (Priem & Butler, 2001; Wernerfelt, 1984). That is, it shifted the emphasis from the external, market and industry-based issues back toward the internal, firm-based factors. Earlier research in strategic management had placed strong emphasis on the competitive environment.

Numerous scholars have contributed to the subsequent development of this resource-based view of strategic management, but the article by Barney is deemed to be the most influential for its attempts to formalize the firm-level, resource-based perspective as a theory and for providing the foundation to many resource-based view studies that followed (Barney, 1991; Priem & Butler, 2001). Barney's organizing framework for explaining competitive advantage rests on two key points: 1) resources are the determinants of firm performance and 2) those resources must be rare (i.e., not widely held), valuable (i.e., improves firm efficiency and effectiveness), inimitable (i.e., cannot be easily replicated by competitors), and nonsubstitutable (i.e., other resources cannot fulfill the same function) to be able to confer a competitive advantage (Barney, 1991; Priem & Butler, 2001). Thus, when a firm possesses rare, valuable, difficult to imitate, and non-substitutable resources, it achieves competitive advantage over other firms. While being rare and valuable are necessary conditions for *gaining* competitive advantage, being inimitable, nonsubstitutable, and nontransferable (e.g., cannot be purchased, etc.) are necessary conditions for achieving a *long-lived or sustained*

competitive advantage (Barney, 1991). Amit and Schoemaker have added other qualities by proposing that a firm's resources are a source of competitive advantage to the degree that they are scarce, specialized, and appropriable (Amit & Schoemaker, 1993).

Barney noted that two assumptions about resource characteristics are axiomatic and elemental to the resource-based view: 1) resources are distributed heterogeneously across different firms in an industry and 2) these resources cannot be transferred from firm to firm without cost (Barney, 1991; Priem & Butler, 2001). Given these assumptions, if a firm's valuable resources are unique to that firm among a group of competing firms, then those resources could generate a competitive advantage for that firm. Barney reasoned that if the value creating strategy that a firm implements is being simultaneously implemented by competitor firms, then competitive advantage cannot exist for any one of these firms implementing the same strategy because they will improve their efficiency and effectiveness in the same way and to the same extent (Barney, 1991). If a firm's critical resources are difficult to replicate and not easily transferable, then the competitive advantage conferred by these resources may be sustainable.

Barney attributes "value" to resources when they can help exploit opportunities and neutralize threats in a firm's environment or when they enable a firm to improve its efficiency and effectiveness (Barney, 1991). In clarifying the value of resources and how such value is determined, Priem and Butler have argued that values are actually determined by demand-side characteristics, which are exogenous to the resource-based view model (Priem & Butler, 2001). Resource values may change as the competitive environment and customer factors change, but resource-based view has simplified

strategic analysis with its assumption of homogeneous product markets and unchanging demand (Priem & Butler, 2001).

According to Caves, a firm's resources are tangible and intangible assets that are tied semi-permanently to the firm at a given time (Caves, 1980). According to Wernerfelt, brand names, in-house knowledge of technology, skilled personnel, trade contracts, machinery, efficient procedures, and capital are all examples of resources (Wernerfelt, 1984). The all-inclusive classification of firm resources as employed by Barney, and based on prior uses and definitions of the term "resources," include all physical assets, infrastructure, workforce, capabilities (e.g., top management skills), organizational processes and routines, firm attributes, information, and knowledge controlled by a firm and that enable the firm to conceive of and implement strategies that improve its efficiency and effectiveness (Barney, 1991; Litz, 1996). Such resources have also been referred to as "strategic assets" (Michalisin et al, 2004). From these ideas pertaining to resources, other views that focus on specific types of resources have been advanced.

Knowledge-Based View

Knowledge-based view of the firm deals with the role of knowledge and its management to offer a rationale for the formation of alliances and provide insight into the nature and management of strategic alliances. The basic presumption of this view is that the purpose of alliances is to facilitate *organizational learning*. The knowledge-based view literature identifies two conceptually distinct dimensions of knowledge management in organizational learning: "exploration," which refers to activities that *generate new*

knowledge to increase an organization's stock of knowledge; and "exploitation," which refers to activities that *deploy and apply existing knowledge* to create value (March, 1991). This distinction has pervaded empirical analysis approaches discussed in the following chapter, in which alliances are being classified as either exploitation or exploration alliances, and various firm attributes are being identified as conditions conducive to proficiency in exploitation versus exploration.

In viewing alliances as vehicles for organizational learning, the presumption that strategic alliances are primarily motivated by firms' desire to acquire the knowledge of their alliance partners has been considered by some scholars to be a very simplistic view. Instead, these scholars have come up with what they call a new "theory of alliances" concerning the role of knowledge in alliances (Grant & Baden-Fuller, 2004). What they have developed, however, is not really a theory but rather a more refined conceptualization that involves a dichotomous characterization of knowledge sharing and transfer between alliance partners, whereby a **distinction is made between knowledge *acquisition* and knowledge *accessing***. Relating back to the knowledge management concept of exploration versus exploitation, these authors explain that knowledge *acquisition* involves using alliances as vehicles of knowledge exploration and learning, whereby each member firm absorbs the partners' knowledge base and *broadens its knowledge base*. Knowledge *accessing* involves using alliances to share knowledge in which each member firm exploits the complementarities in its partners' stock of knowledge, but maintains its distinctive knowledge base and *increases its knowledge specialization*.

Grant and Baden-Fuller suggest that knowledge accessing takes precedence over

knowledge acquisition (for which learning is an integral process) in most strategic alliances because firms want to avoid the problem of underutilizing knowledge that is costly to acquire, because acquiring and learning new knowledge takes time (Grant & Baden-Fuller, 2004). They explain that efficient utilization or application of knowledge can be best achieved when the firm's knowledge domain exactly matches the breadth of knowledge requirements of the firm's product domain with no overlap. Knowledge is subject to economies of scope, to the extent that knowledge is not specific to a single product but can be applied to the development of many sets of products. This could present difficulties for the firm as it must strategically decide which types of knowledge to possess and which types of products to make. From the point of view of efficient knowledge utilization, it would be desirable to have the firm's knowledge resources be utilized to the fullest extent possible; but if products require a broad range and diversity of knowledge, underutilization of knowledge resources is likely to be a problem. That is, internalization of knowledge that is not product-specific but has a wide range of applications in the development of many different products would result in substantial underutilization as the firm would not be developing all those products. Thus, it would not be efficient for a firm to acquire and internally possess all of the different types of knowledge required to produce a certain product if those knowledge resources are to be used in only a couple of the products that the firm supplies.

A firm can avoid carrying excess knowledge capacity by relying upon strategic alliances to access the needed knowledge. In other words, as knowledge integration *within a firm* is associated with increasing marginal costs, efficiency of integration can be maximized *within an alliance* linking separate firms specializing in different areas of

knowledge (Grant & Baden-Fuller, 2004). Thus, the authors propose that a firm will demonstrate greater propensity to form alliances with other firms, the greater the incongruity between the firm's product and knowledge domains. Hence, we would see the number of alliances increase as technology becomes more complex and the range of required knowledge becomes broader. They also suggest that the greater the rate of change of knowledge and uncertainty over future technological changes and knowledge requirements, then the greater are the risk spreading and option creating benefits of alliances under the knowledge accessing approach. Moreover, it has been suggested that early-mover advantage derives less from the generation of new knowledge, as from recombining existing knowledge into innovatory products (Fleming, 2001; Galunic & Rodan, 1998); and this would involve knowledge accessing, as opposed to acquisition. Such knowledge accessing purpose of alliances ties back to the resource-based theory in that knowledge is one of the most important resources of firms.

Insight into knowledge application involves understanding the factors that determine the efficiency and effectiveness with which knowledge is translated into goods and services. Studies of factors that are internal to the firm can be found in the organization science literature, where firms are considered as "social communities" in which economically useful products and services are generated by the application of a set of higher-order organizing principles (Kogut & Zander, 1992). In the **organizational learning** perspective, firms are viewed as organizations of coordination and learning, and they convert specialized knowledge into directives, rules, and operating procedures imposed through authority-based relationships (Grant & Baden-Fuller, 2004). When successful production of goods requires the combination of many different types of

knowledge, then successful knowledge application depends on the ability to efficiently integrate these different types of knowledge. Efficiency in knowledge integration requires coordination that helps preserve knowledge specialization so that high costs of learning in multiple areas can be avoided; and organizational routines of firms provide this coordination that facilitates the integration of knowledge from different specialists (Nelson & Winter, 1982). Such organizational routines are adaptable, but they can also establish paths that produce obstacles and have a constraining effect on the evolution of firm's dynamic capabilities (Teece et al, 1997; Tripsas & Gavetti, 2000).

Competence-Based View

In the 1990's Sanchez developed and introduced a new view under the strategic management theory known as the competence-based view or "competence theory" (Sanchez & Heene, 1997). He argued that the resource-based view offered little insight into the contemporary industry structures in which extended networks of firms simultaneously cooperate and compete. The competence-based view provides a conceptual framework to better integrate the dynamics of a firm's internal organizational processes and its external strategic interactions with other firms. In the competence theory, a firm is characterized as an open system of asset stocks, including tangible assets like equipment and intangible assets like knowledge and capabilities; and the flows within and between firms of these assets are coordinated through management processes for building and leveraging competencies in order to achieve competitive advantages (sanchez, 1996). Because firms may differ in their strategic goals, they are likely to generate distinctive patterns of resource flows as they build and leverage competences.

By investigating the competence building and leveraging objectives of firms, one could come to understand industry dynamics.

Since firms are open systems that depend on resource flows, the competence theory recognizes that firms must collaborate and form competence alliances and networks to support that flow. Firms must constantly replenish their stock of assets through interaction with individuals, other firms, and other providers of resources. Also, since it is rarely the case that any one firm can on its own maintain superior competences in all areas of its competition, firms that are competitors would have incentives to cooperate in building new competences, improving existing competences, or extending the reach of current competences into new markets. The competence theory explains that actions to gain complementary resources allow firms to learn new and valuable capabilities, and that **strategic alliances and networks are an attractive means for accessing complementary assets**. Moreover, it has been posited that while a firm draws on *existing* organizational structure to coordinate *incremental* innovations, more *radical* innovations call for the creation of new resources and a higher intensity of *strategic direction to coordinate complementary* activities. Theory research to build on the competence-based view can involve investigating these interactions between a firm and the resource providers outside the firm (i.e., between competing and cooperating firms).

Dynamic Capabilities Theory

Firms are constantly confronted by new threats to the value of their assets, and **dynamic capabilities** refers to the capacity of an organization/firm to purposefully and systematically create, build, expand, reconfigure, and modify its resources or skills to

address changing environments (e.g., technological context and competitive environment) and changing markets (e.g., markets evolve, die, and new markets emerge) (Eisenhardt & Martin, 2000; Teece et al, 1997). The concept of dynamic capabilities in strategic management theory highlights the crucial role of BOTH organizational factors and contextual/environmental factors in shaping a firm's competitive advantage. **The rationale for testing the interaction effect of age and partner type in this dissertation was based on such influence of changing and dynamic industry environment and recognizing the necessity for alliance networks to evolve over time, with some partnerships dissolving and new partnerships forming.** Since firms engage in alliances in search of capabilities and know-how that they lack internally, certain types of partners may need to be replaced by others as firms mature and their needs change.

An aspect of the dynamic capabilities theory is "path dependency," which was first introduced by Teece in the 1990's and later expanded and expounded by other scholars; and it suggests that a firm's existing capabilities, processes, and routines greatly influence both the kinds of new capabilities it can develop and the rate at which the firm can build new capabilities, and that they often constrain a firm's ability to change its capabilities (Eisenhardt & Martin, 2000; Teece et al, 1997; Zollo & Winter, 2002). These capabilities refer to the firm's ability to build internal competencies and to integrate external competencies in response to technological and market changes (e.g., absorptive capacity). The dynamic capabilities theory is linked to the knowledge-based theory because when firms try to adapt their existing capabilities or to develop or acquire new ones, they engage in a process of learning, and this process is deeply rooted in the firm's existing knowledge base.

All of the theories described above – resource-based, competence-based, and knowledge-based views and the dynamic capabilities theory – present interrelated but slightly different insights into why and how alliances are strategically important for organizational learning and efficient translation of knowledge into the production of new goods and services, i.e., for *innovation*. Strategic alliances provide a mechanism for firms to develop new competencies and evolve their dynamic capabilities (learned patterns of collective activity) (Zollo & Winter, 2002). This dissertation builds on and enriches the strategic management literature by attempting to identify alliance and network characteristics and dynamics that make alliances more effective as vehicles for knowledge management (i.e., creation, transfer, and application of knowledge).

Network Theory

Networks have been studied by sociologists for many years, and recently networks have become the subject of great interest to the scholars of technology innovation. Network theory in the context of biomedical technologies is pertinent because its premise is that firms need to form networks of learning in order to cope with increasingly complex knowledge base required for modern technologies. Network theory says that the formation of linkages between firms facilitate the combination of diverse knowledge that relates to technology, organizational practices, and market trends (Goerzen, 2007), and that learning derived from diverse connections yields benefits to the firm (Beckman & Haunschild, 2002; Laursen & Salter, 2006). This has been particularly apt for the biotechnology industry, whose accelerating pace of technological advances has been accompanied by a decentralization of the sources of technological knowledge.

Powell et al. go so far as to argue that as the knowledge base of an industry expands and grows more complex, where sources of expertise are broadly dispersed, the *locus of innovation is within networks* of learning *rather than in individual firms* (Powell et al, 1996).

One area of network research deals with the ties between familiar partners and aspects of those ties that mediate efficient relationships. Scholars have suggested that networks develop as those with established relations try to find new ways to work together (Gulati, 1995). Through interpersonal ties across organizations, a greater understanding of each other's needs and capabilities, and opportunities for new alliances emerge (Goerzen, 2007). Although there exists some competition versus cooperation tension in dealing with transaction costs (Hennart, 1988), the development of trust between familiar partners in alliance networks reduces transaction costs, which include search and monitoring costs and knowledge transfer costs, and makes the existing relationships efficient and easy to maintain (Dyer & Chu, 2003; Gulati, 1995). In other words, alliances foster investments in trust, which can help limit opportunism (Ring & Vandeven, 1992; Simonin, 1997). Zollo et al. have suggested that repeated ties might allow for more convenient routines that facilitate the day-to-day operations of an alliance and result in a positive attitude of managers toward the alliance (Zollo & Winter, 2002).

Another focus of network research in the recent years has been on network structures and the influence of a firm's position within a particular structure on its performance. Network positions have been classified primarily into two different types: a "position of prominence" and an "entrepreneurial position" (Koka & Prescott, 2008). A firm in a position of prominence or network centrality is well-connected through multiple

direct links with other firms, and derive network benefits that include 1) greater access to key information and 2) opportunities to establish the firm's own strategic agenda as the defining norm in the industry and to control the trajectory of new knowledge created in the network (Koka & Prescott, 2008). One measure for network centrality to capture the extent to which the firm is connected to other central firms is an eigenvector-based measure calculated as the weighted sum of the centralities of the firm's partners (Bonacich, 1972). A firm in an entrepreneurial position acts as a bridge between different parts of the network that are otherwise unconnected and exists in a network characterized by multiple "structural holes" (i.e., characterized by lack of ties among the firm's partners) (Koka & Prescott, 2008; Zaheer & Bell, 2005) Benefits derived from being in an entrepreneurial position include 1) exposure to information *diversity* and 2) opportunity to synthesize diverse information into novel combinations that enable exploration into new markets (Burt, 2000; Koka & Prescott, 2008). One way that entrepreneurial position has been operationalized is through the structural holes measure. Many structural holes indicate that the network members are unconnected to the other members and this can be calculated from the value for "constraint" using a software program for social network called UCINET V (Koka & Prescott, 2008). High constraint indicates that the partners are densely connected to one another, while a low constraint indicates a sparsely connected network.

Since the two types network positions enhance competitive advantage through different benefit streams, Koka and Prescott examined how each would affect firm performance in response to changes in the industry environment (e.g., new legislation, introduction of a new technology) (Koka & Prescott, 2008). They focused on the steel

industry and analyzed data from a sample of 70 firms that formed at least one alliance during 1983-1993. Surprisingly, they found that in response to a technological change, the firms that were prominent in the network suffered a decline performance – measured as sales per employee – compared to those firms that were not prominent. Firms maintaining an entrepreneurial position also exhibited lower performance relative to the other firms (Koka & Prescott, 2008). Holding strategic positions in these network structures failed to enhance firm performance. On the other hand, when Powell et al. mapped the network structure (i.e., connection of firms to each other) of the biotechnology industry to better understand organizational learning and the purposes served by the extensive connections that characterize this field, they found that firms with ties grew faster than those without ties (Powell et al, 1996). Further adding to these variant and somewhat conflicting findings, others scholars have found that a network structure with multiple structural holes was associated with higher innovativeness (Zaheer & Bell, 2005).

Network theory is interrelated to the aforementioned theories of strategic management in that network externalities include complementarities and transaction efficiency advantages, and they are enhanced in the face of uncertainty over future knowledge requirements for product innovation. Many scholars have conducted empirical research to validate the value of forming alliances and networks with research universities and with other firms as sources of new knowledge, and to elucidate the role these partners may have on firm performance. Earlier works have resulted in diverse and sometimes conflicting conclusions about partnership characteristics to which greater firm success could be attributed, and these studies are reviewed at length in Chapter 4.

CHAPTER 4: REVIEW OF EMPIRICAL STUDIES ON PARTNERSHIPS

There is extensive literature providing theoretical and qualitative assessments of the strategic benefits as well the risks of R&D linkages for firms belonging to technology-based and science-based industries. Other more recent studies have carried out empirical analyses on the impact of such linkages on firm performance and success. The strategic benefits cited frequently in the economics literature include the capture of knowledge spillovers by member firms; reduction of duplication of investment and effort; complementation of scientific and technological strengths; and exploitation of research synergies and economies of scale. Additional rationales or incentives for collaboration specified in the literature include *sharing R&D costs and risks*, accessing and pooling diverse specialized expertise and complementary skills to better *deal with complexity* and evolving knowledge needs, making up for deficiencies in internal capabilities and resources, *accessing new technologies and markets*, *learning* from partners (e.g., about new technologies, ways in which technological change may affect the business, and about better organizational approaches), co-opting competition, creating new options, and expediting time to market, all of which could help reduce innovation time span (Arora & Gambardella, 1990; Eisenhardt & Schoonhoven, 1996; Hagedoorn, 1993; Hagedoorn et al, 2000; Harrison et al, 2001; Kleinknecht & Reijnen, 1992; Mowery et al, 1998; Standing et al, 2008). The risks include opportunistic exploitation by partners, coordination costs, and loss of control of important assets (Hamel, 1991).

Scholars have even developed "taxonomies" of R&D collaborations to classify the types R&D collaborations. Mowery, for example, groups them into three categories:

industry-led consortia; university-industry collaborations; and collaborations between federal laboratories and industry (Mowery, 1998). The literature, for the most part, can be broadly grouped into studies of university-industry collaborations and interfirm collaborations, as described further in this chapter.

Impact of University-Firm Linkages on Innovation

It is generally acknowledged that university-generated knowledge laid the foundation for the genesis of biotechnology industry, and without advances made through academic research many industrial innovations would not have been realized (Beise & Stahl, 1999; Mansfield, 1991). Hence, there has been tremendous scholarly interest in understanding the strategic importance of maintaining linkage with universities as an external source of new knowledge for firms. Through **case history** of a sample of high therapeutic impact drugs introduced between 1965 and 1992, Cockburn and Henderson demonstrated the important role that public sector research had for the pharmaceutical industry in providing the key enabling discoveries for the development of those drugs (Cockburn & Henderson, 1998). Numerous other studies have provided **qualitative assessments** of the strategic benefits to establishing close linkages with research universities, such as gaining access to 1) emerging, cutting-edge scientific advances and knowledge; 2) research resources and equipment in university laboratories, and 3) human capital in the form of cheap student labor and faculty consultants, as well as enhancement of the company's legitimacy in the eyes of other stakeholders (Geisler, 1995; Gluck et al, 1987; Lepkowski, 1996; Mian, 1997; Peters et al, 1998). For university scientists, links with firms can provide opportunities to develop and test their theories, as well as sources

of funding to pursue important R&D projects (Cyert & Goodman, 1997). However, according to Cyert and Goodman, conflicts between the university and business cultures can decrease company performance (Cyert & Goodman, 1997).

In the recent years, there have been abundant **empirical studies** on the impact of linkages with universities on firm performance and success. They have used various measures, such as firm growth, revenue generation, return on sales, publications, patents, products in development, and products in market, to determine firm performance. As described below, however, the outcomes of studies to establish the importance of university-firm collaborations have been inconsistent. Zucker and Darby have shown through econometric analysis of co-authorship data of the biotechnology industry in California that "star" scientists played a key role in the development of biotechnologies and their successful commercialization (Zucker & Darby, 1998). That is, firms tended to have more products in development and in the market when they had greater number of jointly authored articles with star university scientists. Star scientists were defined as those who by 1990 (a cutoff date before the perfection of sequencers that could inflate the number of sequences that a scientist could "discover") had recorded more than 40 genetic sequence discoveries or had authored at least 20 articles reporting such discoveries. Their explanation for the findings was that new knowledge, at least in the breakthrough stage, was embodied in particular individuals. Such knowledge had important tacit elements that must be learned by working with the scientists who made the discoveries and could not diffuse rapidly through duplication of protocols. Cockburn and Henderson measured firm performance in terms of the number of "important" patents, "importance" being defined by the patent being granted in at least two out of three world markets (i.e., U.S.,

Japan, and Europe), and have shown that the fraction of coauthorships with universities had significant effect on research productivity of the firms (Cockburn & Henderson, 1998). Various other scholars have also demonstrated that firm-university alliances can increase a firm's innovative outputs, as measured by the number of products created or patents obtained (Austin, 1993; Deeds & Hill, 1996; Liebeskind et al, 1996).

While the aforementioned studies demonstrated that university-firm linkages improved firm performance, other studies showed that university-firm linkages did not improve *market* performance or innovation. George et al. examined the effects of university-firm alliances on the performance of 147 publicly-traded biotechnology companies and showed that firms with university linkages had greater number of patents and lower R&D spending than firms without such linkages (George et al, 2002). However, their data failed to demonstrate any statistically significant association between university linkages and the number of products under development or on the market. Also, these companies did not achieve higher financial performance compared to similar firms without university linkages. According a study by Colombo and Delmastro in Italy, university-based start-up companies were found to have a slightly easier time gaining access to public subsidies and adopting advanced technologies, but they were not found to be any more innovative or higher performing than independent start-up companies (Colombo & Delmastro, 2002). Similarly, scholars focusing on the origin of new firms found no difference in innovation between university-based start-ups and independent high-technology start-ups with regard to the number of new products and services launched (Westhead, 1997). It should be noted that university-based start-up firms are likely to have ties and privileged access to university research while independent start-

ups are not likely to have a history of university ties. Also, Laursen and Salter found only partial support for the hypothesis that firms that rely more on university R&D sources are more innovative in terms of product innovations (Laursen & Salter, 2004). Others studying European firms found no support for such a hypothesis, in that innovation intensity was not significantly related to collaborations with universities or government labs (Mohnen & Hoareau, 2003).

Types of enterprises that forge links with universities

The previous section contained a review of studies investigating the benefits from R&D links with universities. In this section, studies delving into the attributes of firms that tend to collaborate with universities are summarized. There have been many studies focusing on the role of firm size in influencing the propensity of firms to collaborate with universities, but conclusions on whether it is the large or the small firms that benefit more from university knowledge spillovers have been mixed. For example, several scholars found that **small firms** benefited more from university-based research spillovers than large firms (Acs et al, 1994; Link & Rees, 1990).

On the other hand, when Mohnen and Hoareau used the results from the second European Community Innovation Surveys (CIS 2) (data from manufacturing sectors in France, Germany, Ireland, and Spain) to investigate the types of enterprises that forge close links with universities and government labs, they found that **larger firms** were more likely to source knowledge from universities (Mohnen & Hoareau, 2003). Their firms belonged to sectors that included chemicals (not pharmaceuticals), machinery and equipment, motor vehicles, electrical and electronic products, telecommunications,

computer services, and engineering services. Direct collaboration with universities and government labs was characteristic of large firms, and the authors' explained that large firms were more likely to have the means to set aside a budget for collaborations with basic science institutions.

Fontana et al. used the results of KNOW (Knowledge Flows in European Industries) survey of small and medium-sized enterprises (SMEs) from low to high technology sectors in seven European Union countries to study the "determinants" (i.e., firm characteristics) of collaboration with universities, measured in terms of the propensity to collaborate and the extent of collaborations (Fontana et al, 2006). The SMEs were limited to the following five sectors: 1) food, 2) chemicals (excluding pharmaceuticals); 3) communications equipment; 4) telecommunications services; and 5) computer services. What they discovered was that the propensity to forge a collaboration with academic partner depended on the size of the firm, with **larger firms being more likely** to collaborate. In addition, firms that had more intense R&D activities (including outsourced R&D) and *patented more* showed higher levels of R&D cooperation with universities. Interestingly, Panagopoulos provided empirical evidence that firms that chose to *have minimal intellectual property protection* were more likely to collaborate with universities (Panagopoulos, 2003).

Not all firms choose to collaborate with universities. There are industrial sectors as a whole, for which collaborating with universities isn't a common practice. By interviewing firms, Fontana et al. have been able to compile a list of reasons that firms cited for not collaborating with universities, and they are as follows: discrepancies between the objectives of the two parties, the length of time involved in university

research, the different focus and different research questions addressed by universities and firms, cultural differences, and uneasiness with disclosure procedures of universities (Fontana et al, 2006).

Impact of Interfirm Linkages on Innovation

There have also been numerous studies focusing on the impact of interfirm linkages on firm performance, and the benefits reaped from them. Interfirm linkages have been characterized by scholars in various ways. For example, Hagedoorn has grouped interfirm alliances as being *technology-oriented versus market-oriented* (Hagedoorn, 1993). Other scholars have examined performance implications of *R&D alliances versus commercial alliances*. Still others have characterized alliances as *exploitation alliances versus exploration alliances* (Levinthal & March, 1993; Rothaermel, 2001). The types of alliances formed by incumbent pharmaceutical firms, for example, have been classified as being overwhelmingly (2:1) exploitation alliances to exploration alliances, with the vast majority of them (87%) being non-equity alliances (Rothaermel, 2001). Baum et al. have categorized the alliances into *horizontal alliances* with other biotechnology firms; *vertical-downstream alliances* with pharmaceutical, chemical, and marketing firms; and *vertical-upstream alliances* with universities, research institutes, government laboratories, and hospitals (Baum et al, 2000). While alliances with *upstream* partners help generate new scientific ideas and provide access to technological know-how (Powell et al, 1996), alliances with *downstream* partners provide access to complementary assets critical to successful development and commercialization, such as expertise in managing clinical trials, production facilities, marketing and distribution infrastructure, and market

access (Baum et al, 2000; Pisano, 1990).

There is ample literature citing that learning from alliances and networks with other firms can improve the growth, success, and ability (to develop new products) of small, entrepreneurial firms in high-technology industries (Bartmess & Cerny, 1993; Baum et al, 2000; Chell & Baines, 2000; Gulati, 1998; Lechner & Dowling, 2003; Shan et al, 1994). Shan et al., for example, have demonstrated that cooperative ties established by U.S. biopharmaceutical start-ups with commercial firms positively influenced their cumulative innovative output, as measured by the number of patents issued (Shan et al, 1994). Studies on interfirm partnerships have determined that the predominant motive for strategic partnering with other firms is to access resources, capabilities, and tacit knowledge (Gulati, 1998; Hagedoorn et al, 2000; Mowery et al, 1998; Teece, 1992). In particular, capabilities that are **complementary** to those that the firm already possesses have been the focus of many studies on partnerships and alliances. Harrison et al. showed that resource complementarity, as opposed to similarity, was associated with *higher performance* in business acquisitions (Harrison et al, 2001). Rothaermel conducted an empirical study to demonstrate the importance of interfirm cooperation for large pharmaceutical incumbents in enabling them to adapt to radical technological changes (Rothaermel, 2001). Upon analysis of 889 strategic alliances between pharmaceutical companies and new biotechnology firms, he showed that the large incumbent firms' alliances with providers of new technology were *positively associated with the incumbents' new product development*. He also showed that these interfirm alliances tended to leverage the incumbents' complementary assets.

Partnering with other firms to build competencies in the *development* process is

what could be described as strategic use of network relationships to overcome the "liabilities of newness and smallness" (Dowling & Helm, 2006; Freeman et al, 1983). Competencies in product development would be complementary assets sought out by younger firms. Dowling and Helm focused on the importance of collaborations for product development success of 60 firms in the high technology region around Jena in Germany, and found that younger firms were more successful when they collaborated with other firms, while older firms benefited more from cooperation with research institutions. Their sample of firms was divided into an "old" group and a "young" group, at the median value for firm age: young (founded during the 5 year time period between 1996 and 2001) versus old (founded during the 5 year time period between 1990 and 1995). Their findings were based on 60 survey responses from firms with an average number of 66 employees. Their measure of success was "market" success, as defined by the percentage of new product ideas that were successfully brought to market in the form of new products. The "cooperation" measure or partnership characteristics was also divided into 2 categories -- "mostly with other firms" versus "mostly with scientific institutions" -- based on the survey respondents' selection of one or the other of these choices. What was surprising was their finding that, in the absence of grouping the firms into the two categories (young vs. old), having cooperative relationships with other firms had a negative effect on the percentage of a firm's innovative products as did having cooperative relationships with universities. A similarly puzzling finding by Koka and Prescott, in which firms that had many ties with other prominent firms in the network exhibited worse performance in terms of sales than firms that were not well-connected was discussed in the previous chapter (Koka & Prescott, 2008). It should be noted that

Dowling and Helm's use of a variable to represent mutually exclusive conditions such as "mostly other firms" versus "mostly scientific institutions" may not have been appropriate. Such dichotomous network patterns were not observed for bioscience and biotechnology firms analyzed in this dissertation, which had collaborations with many firms and many academic institutions concurrently.

Liebeskind noted that by allying with potential *rivals*, start-ups could gain access to uncodified, tacit knowledge about strategy, technology, and operations critical to their success (Liebeskind et al, 1996). When Baum et al. examined the impact of alliance network composition at the time of founding on start-ups' performance in the Canadian biotechnology industry, they found that forming alliances with potential *rival* biotechnology firms **weakened and was detrimental to firm performance** because of intra-alliance rivalry (Baum et al, 2000). The exceptions were partners who were highly innovative (i.e., had high rates of patenting). Their study involved 142 Canadian biotechnology firms founded during 1991 to 1996, and the measures of performance up to six years post-founding included revenue growth, employment growth, R&D spending growth, and patenting rate.

Factors that Influence Partner Selection

In another stream of strategic alliance research literature, factors that influence partner selection have also been the subject of much scholarly work. Partner selection for strategic alliances involves more than simply choosing the firm with the best skills or resources, and scholars have been trying to understand when and why certain partners would be deemed attractive. Some of these factors include characteristics such as partner

reputation (Dollinger et al, 1997), partner complementarity (Hitt et al, 2004), and trust, which has been identified as helping to minimize uncertainties and reduce the threat of opportunism in strategic alliances (Das & Teng, 1998; Gulati, 1995; Nooteboom et al, 1997; Zaheer et al, 1998). Hitt et al. have examined the stage of economic and market development as a moderator of the influence that various factors have on partner selection (Hitt et al, 2000). Others have examined partner attractiveness vis-a-vis characteristics that would be best suited for a particular alliance *project* (Shah & Swaminathan, 2008). In other words, they focused on the alliance project type as a moderator of the influence that the aforementioned factors have on partner selection.

Shah and Swaminathan posited what makes a partner attractive would vary depending on the alliance project type, and managers would value certain partner characteristics more than others (Shah & Swaminathan, 2008). The project types were characterized on two dimensions: process manageability and outcome interpretability. Process manageability referred to how easy or difficult it would be to manage the implementation process, such as the interactions and coordination needed to accomplish the alliance project. The costs of alliance governance, in terms of the management time invested by the partners, the number of other personnel involved in the alliance, and the amount of their energy expended were taken into consideration. Outcome interpretability referred to how transparent and readily interpretable the outcome of the project was. Outcomes could be difficult to interpret when the evaluation of outcome is subjective in nature, or there might be difficulties in attributing the benefits to the alliance, as when the outcome involves performance variables such as learning or when there is difficulty translating the outcome to a dollar value.

Shah and Swaminathan hypothesized that when process manageability and outcome interpretability are low, trust is more important as the basis for partner selection than complementarity or other factors; when process manageability is high but outcome interpretability is low, the most valuable is complementarity (Shah & Swaminathan, 2008). These hypotheses were tested through an experimental approach that involved creating hypothetical scenarios based on real ongoing alliances between a major U.S. airline and its partners. The scenarios were developed to reflect different strategic alliance project types in terms of process management and outcome interpretability. Managers who had experience in evaluating and selecting partners were randomly assigned to review one of four different scenarios and respond to indicate how critical different partner characteristics (e.g., trust, complementarity, financial payoff) were on partner attractiveness. The results of their analyses supported their hypotheses.

Impact of Redundant and Non-Redundant Partnerships

From the network theory perspective, firms have an incentive to improve their competitive position by expanding the reach of their networks, through non-redundant ties (Granovetter, 1985). The rationale is that firms with diverse ties have access to a variety of ideas, perspectives, and knowledge that firms with primarily redundant contacts do not. Similarly, Baum et al. have suggested that growth in alliance network may not be helpful if redundancy in the partner function results in access to the same information from different partners, and that a more ideal composition would be to have partners that each provide different complementary capabilities (Baum et al, 2000). Moreover, it has been argued that the costs associated with redundancy in multiple

partnerships will make networks inefficient (Baum et al, 2000). In a recent study that examined the effect of repeated partnerships on the performance of Japanese multinational corporations, firms that engaged in equity-based partnerships repeatedly with the same partner experienced inferior economic performance (Goerzen, 2007).

In practice, however, firms often enter into repeated alliances with prior partners because of the trust and familiarity that develops between partners and reduced transaction costs, as noted in the previous chapter. Beckman et al. have argued that when uncertainty is high, firms will choose to form relationships with previous partners (Beckman et al, 2004). Hagedoorn has observed that strategic technology alliances create steady networks of cooperating companies in which a "core" of heavily partnering companies remain intact (Hagedoorn, 1995). And numerous other scholars have concluded that networks with greater inter-organizational tie redundancy develop more efficient alliance governance arrangements that lead to superior firm performance (Dyer & Chu, 2003; Gulati, 1995; Zollo & Winter, 2002). Unfortunately, many studies in the alliance literature did not clarify whether the alliance count included repeat alliances, and this could be one possible source of the discrepancies in the conclusions that had been reported about network's role in firm performance.

Intrafirm Processes for Alliance Learning

While the preceding sections dealt with literature on the characteristics of networks and the impact of different types of partnerships, this section discusses **intrafirm** processes that take place within the context of alliances to explain how learning occurs and how firm capabilities are developed **within a firm**. These intrafirm

processes have an important role in facilitating firm success although they are not represented by variables examined in this dissertation study, which may constitute one of the limitations of this dissertation. Nonetheless, they are reviewed here because knowledge management, particularly management of relationships after an alliance has been formed, is key to optimally deriving benefits from alliances.

Certain firms are more adept at managing alliances – identifying partners and valuable alliance opportunities, initiating and successfully negotiating these alliances, and managing partner expectations. So, how do they develop or acquire these abilities? We know that alliances can provide access to new knowledge, but how do firms effectively take advantage of this opportunity? According to Kale and Singh, alliance learning occurs through a process that involves articulation, codification, sharing, and internalization of alliance management know-how, and a firm that can incorporate and put this process into practice has greater alliance success (Kale & Singh, 2007). Therefore, firms that have a dedicated alliance function (e.g., a dedicated staff/office) that oversees and coordinates their overall alliance activity have greater alliance success (Anand & Khanna, 2000; Draulans et al, 2003; Kale & Singh, 2007). In fact, a direct, positive relationship between alliance function and alliance success, in which "alliance success" was measured through managerial assessment and scoring of alliance performance, had been observed previously (Kale et al, 2002; Kale & Singh, 2007).

Among the processes that Kale et al. have outlined, communication has been regarded by some scholars as being one of the most critical for deriving benefits from an alliance (Standing et al, 2008). Standing et al. developed a framework for managing the creation and transfer of knowledge related to strategic alliances within the context of the

Australian biotechnology industry and noted that it is influenced by factors such as absorptive capacity and communication competence (Standing et al, 2008). These authors have pointed out that a dedicated alliance management team functions to enable easier communication and resource access across interorganizational boundaries, and that communication is important for building the necessary commitment and trust between partners. Relatedly, other scholars have noticed that perhaps because collaborations allow firms to gain valuable experience in responding to new opportunities, alliance management is placed at the core of corporate functions by many firms (Dodgson, 1996; Kogut, 1991).

CHAPTER 5: RESEARCH QUESTIONS

The primary objective of this dissertation research is to investigate the influence that R&D alliances have on the ability of firms to successfully innovate products. Why do some firms achieve greater innovation success than others? Could the success enjoyed by some firms be explained by their R&D alliances as one of the contributing factors? It has been recognized by the scholars of biotechnology industry that the formation of strategic alliances is critical for small biotechnology firms to develop as viable entities (Standing et al, 2008). That being the case, how important for innovation success are interfirm partnerships, collaborations with universities, and clinical ties? Recent empirical studies of alliances reviewed in the previous chapter have focused primarily on interfirm or firm-university partnerships to evaluate the role of these partner types in contributing to various aspects of firm success, and such approach has guided the classification of *partner types* in this dissertation research into *firm* (or corporate) partners, *university* (or academic) partners, and *clinical* partners.

The research questions for this dissertation are as follows. The first two research questions are addressed by specific hypothesis testing through inferential statistics, and the third question is addressed by descriptive statistics and data summarization.

1) To what extent can collaborations with different partner types explain product/process innovation success by small bioscience firms.

2) How does firm age (i.e., stage of maturity) moderate the role that different

partners have on innovation success.

3) How do R&D network characteristics of small firms differ among the three bioscience sectors representing biotechnology, pharmaceuticals, and diagnostics. That is, do firms belonging to these different bioscience subsectors differ with respect to the type of partners they preferentially select (perhaps due to differences in the level of technology or the development pathways involved in what they produce).

According to scholarly works from the alliance literature, the predominant motive for forming partnerships is access to resources, capabilities, and tacit knowledge (Gulati, 1998; Hagedoorn et al, 2000; Mowery et al, 1998; Teece, 1992). The resource-based and competence-based theories from the strategic management literature, which focus on the competence building strategies of firms through resource flows and access, add another dimension to the study of alliances. They do so by emphasizing that key to effectiveness of strategic alliances is access to *complementary* knowledge, capabilities, and resources. In other words, we can draw from the competence-based view of the firm that by leveraging *partner complementarity* and learning from it, firms can build competencies that form the basis for improvement in firms' ability to innovate new products. Scholars have noted that complementarity, compatibility and relational capital often form the basis for strategic alliances (Sarkar et al, 2001); and past studies of cooperation between new entrants and incumbent firms in the biotechnology industry in the commercialization of new technologies were also framed by this concept of complementarity (Pisano, 1991;

Rothaermel, 2001).

These prior works have provided the theoretical framework for this dissertation's examination of the innovation advantages provided by different types of partners in an alliance network, whereby consideration of complementarities that would be competence building for small bioscience firms has been a driving force in the formulation of the specific hypotheses presented here. It is argued in this dissertation that with a view toward translating scientific knowledge and discovery research results into concrete products, the know-how and tacit knowledge required for innovation can best be gleaned from networking with other firms rather than with universities, and preferably with firms that are more established and experienced in advancing product development and commercialization. Standing et al. have noted that biotechnology firms, especially at the start-up stage, lack the necessary business knowledge and skills (Standing et al, 2008), and again the best external sources of these competencies might be other firms.

Hypotheses

Hypothesis 1: Young bioscience firms that engage in a greater number of firm-firm collaborations are more successful at product/process innovation than those that engage only or predominantly in firm-university collaborations.

This hypothesis tests the argument that **interfirm** alliances would be particularly beneficial and important for **young** firms. The strategic needs and motives of small and young biotechnology enterprises may be quite different from those of pharma giants and

well-established biotechnology firms. As Baum et al. explain, the establishment of alliances with other firms at the time of founding could significantly mitigate the risks of newness and reduce the hazards faced by start-ups because the knowledge, stability, and associative legitimacy that the partners confer on the start-up can compensate for the disadvantages of organizational inexperience (Baum et al, 2000). When we consider such deficiencies of start-ups and young firms as a group, it seems that corporate partners, more than any other types of partners, would possess the most needed complementary knowledge and resources.

Older firms, on the other hand, are more likely to need external sources of scientific knowledge for fresh ideas, whether those sources be universities or start-up companies. As described in Chapter 2, it is well-documented that alliances between biotechnology start-ups and pharmaceutical incumbents were crucial and inevitable during the initial, burgeoning phase of the biotechnology industry, when the established pharmaceutical companies turned to the biotechnology start-ups to access radically new scientific and technological breakthroughs (McKelvey et al, 2003; Orsenigo et al, 2001; Roijakkers & Hagedoorn, 2006)

Some scholars have argued that new firms suffer a disadvantage with respect to the incumbent firms in the assimilation and exploitation of publicly available generic and less targeted knowledge (Breschi et al, 2000). It has also been said that small firms often face serious problems benefitting from R&D collaborations because the participating firms must have resources to make significant investments in technology absorption (Mowery et al, 1998). The notion behind "absorptive capacity" – defined as the ability to evaluate and assimilate new knowledge – is that you need to perform R&D yourself in

order to support the inward transfer and capture of academic knowledge and R&D results, such that only firms that invest in in-house R&D are able to extract knowledge from basic research institutions and collaborative R&D projects (Cohen & Levinthal, 1989; Cohen & Levinthal, 1990).

While such statements on the deficiencies of new and small firms may be true for the firms belonging some other sectors, they are not at all generalizable to the bioscience start-ups. The belief that small firms are somehow less able to perform in-house research could not be farther from the truth for those belonging to the bioscience sector. First of all, the companies that are most closely in touch with academic research and that have greater absorptive capacity would be the newer, smaller companies. As Standing et al. have accurately observed, many biotechnology firms are small companies that develop from scientific research carried out in universities and these companies have a scientific focus with scientists as key personnel (Standing et al, 2008). In other words, many start-ups are spin-outs from universities and are founded by scientist-entrepreneurs out of university laboratories. Moore, who focused specifically on biotechnology companies, has even described these small companies as being at the academic interface (Moore, 2003). Secondly, whether small or large, firms in this sector as a whole are highly knowledge-intensive and research-intensive. Hiring scientists and researchers with relevant scientific knowledge base is a common practice in the biotechnology industry, even though scholars such as Cockburn, Henderson, Zucker, and Darby might make the argument that it is *not enough to simply hire* expert scientists and that firm researchers must be actively collaborating with public sector researchers in order to be innovative.

Hypothesis 2: Bioscience firms having ties with large corporate partners in their alliance network are more successful at product/process innovation than those that do not have such ties.

The benefits of interfirm linkages and the reasons why they help improve firm performance as explained in the literature by various scholars are that partnerships with other corporate partners allow small businesses to make up for deficiencies in their own capabilities and resources by accessing the know-how, the technologies, and the markets of their partners. If such were the case, then even greater benefits could be reaped from collaborating with larger, **well-established firms** than with smaller firms. The know-how and tacit knowledge required for innovation success, in particular, could best be acquired by forming alliances with firms that are more experienced in product development and commercialization processes. While many of the bioscience and biotechnology firms already possess adequate internal *research* competencies to generate novel scientific discoveries in-house, not all firms would have the core competencies that the more established firms possess as a result of cumulative experience. These core competencies would include proficiency in managing the *development processes*, such as clinical trials and the regulatory hurdles imposed by the FDA. The notion that not all interfirm alliances may contribute positively to firm performance and that the complementary assets needed by these small biotechnology firms may be found in the more prominent, established firms is tested through this hypothesis. Interfirm alliances are further classified in this dissertation to distinguish those alliances with large firms, and this partner firm size attribute is used as a proxy measure for possessing the requisite

experience that has enabled the firm to successfully grow and become well-established in the industry.

Hypothesis 3: Firms that collaborate with clinical partners (e.g., hospitals, clinics, medical centers) are more likely to succeed in the innovation of products subject to the FDA regulations than firms that lack clinical partners.

Hypothesis 3 is based on the rationale that firms making FDA-regulated products (i.e., therapeutics and devices intended for use in the diagnosis of disease or other conditions, or in the cure, treatment, prevention, or mitigation of disease – the Food, Drug, and Cosmetic Act, 21 U.S.C. 321(h)) can shore up internal deficiencies in clinical development know-how by accessing the complementary skills available at clinical institutions that routinely engage in and oversee clinical research. In addition to exploring the impact that firm-clinic linkages may have on product innovation success, this hypothesis also examines the interaction effects of FDA regulation on the impact of the clinical collaborators on innovation success. As explained in Chapter 2, some of the greatest challenges and hurdles to the successful development of many biomedical products reside at the level of clinical validation and regulatory compliance. New products designed for use in humans or for making treatment decisions are distinct from other products entering the marketplace in that the law requires that they must undergo extensive clinical testing for safety and efficacy and premarket approval by the FDA before they can be marketed. Coordinating large-scale, multi-center clinical trials involving complexities in patient accrual, informed consent, and data management

presents enormous challenges for therapeutic product development. Building relationships with clinical experts who are experienced in designing and enrolling patients into clinical trials could benefit firm researchers trying to navigate and manage this process. Perhaps because this development process is unique to the biomedical sectors, there is a dearth of studies on the contribution of clinical entities to biotechnology innovation and the value of their inclusion in R&D partnerships. Exploring the effect of firm-clinic linkages is a unique contribution of this dissertation to the literature.

Hypothesis 4: There is a positive relationship between research output productivity, as measured by publications and patents generated, and innovation outcome.

Testing this hypothesis on the a*ssociation between research output and innovation outcome* has been made feasible by the available data. This hypothesis deals with the relationship between short-term R&D outputs and long-terms outcomes. Many previous studies found in the literature have used the number of publications and patent counts as indicators of firm productivity from which the authors have proceeded to draw conclusions about firm performance. Such output values are frequently used because they can be obtained independently and quite easily by researchers, without having to survey or interview firm employees. So, how well can publications and patents serve as surrogate measures for innovation success? How strong is the relationship between the numbers of publications and patents that result from a project and success in

commercializing the final product? This analysis assesses the validity of a commonly practiced research methodology, whereby output measures are frequently employed as proxy measures of outcome in cases where the outcomes are difficult to measure.

It is reasonable to think that a more productive firm generates more research findings to publish and develops more novel product ideas to patent. Strategic patenting and intellectual property protection are critical for developing a product that will have market viability and for demonstrating to potential investors the likelihood of firm's success, but patents do not always lead to marketed products. What really matters is the ability of firms to get products to the market and the success of those products to remain in the market, not merely the number of publications or patents that the firms amass. It remains to be determined whether these outputs are intermediates to outcomes or whether such achievements are somehow independent of achieving the outcome success of placing products in the market.

A Focus on Diagnostics

Finally, this dissertation also examines how biotechnology, pharmaceutical, and diagnostics industries differ from each other with respect to the distribution of the types of R&D partners in the networks formed by small businesses within these industries. The partnering behavior of diagnostics companies is of particular interest due to a lack of studies reported on firms in this category. Diagnostics is primed to have a central role in personalized medicine (i.e., therapy that is tailored to the most effective combination of drugs targeting the specific biological makeup of a disease), which is increasingly becoming the subject of public interest. The emerging pharmacogenomic technologies

are bringing the promise of targeted therapies within reach, and creating new opportunities for diagnostic companies to develop tests that can be used to determine patient responses to drugs and to screen out inappropriate candidates. A likely scenario is for diagnostic tests to enable the selection of one of several therapies, or serve as a prerequisite to prescribing a therapy such that diagnostics would be the gateway to therapeutics. Widespread adoption of pharmacogenomic testing and other means of personalized medicine could mean that diagnostic companies will need to formulate business models and strategies that involve forging mutually beneficial partnerships with pharmaceutical and biodrug companies.

CHAPTER 6: METHODS

All pertinent scientific papers published and patent applications filed by each SBIR grantee firm between the first year of the SBIR award and 5 years post-award were researched and co-authorship data systematically analyzed in order to identify the firm's R&D collaborators. Once all the collaborators have been identified this way, each collaborator was characterized into a partner type. A 5-year time frame post-award was chosen to take into account that the duration of the SBIR award may be up to 3 years and it could take an additional year after the completion of project to prepare a manuscript and another year after that for the publication to appear in a journal. The resulting data provided a list of all partners that defined the R&D alliance network that the firm had built around itself during the time that the SBIR project was being carried out. **These partnership data were then subjected to multiple inferential statistical analyses** involving logistic regression models with innovation outcome as the dependent variable.

Data Sources

There were two data sources for this dissertation project: 1) responses from the SBIR Program evaluation survey conducted in 2002 by the NIH, and 2) publications and patent applications by these SBIR grantees. **The questionnaire that was used in the survey (OMB Control No. 0925-0499) is included in Appendix A.** This survey was followed up with an Outcomes Update Survey in 2006 to obtain updated responses and data, which were included in the data analyzed for this dissertation. The SBIR questionnaire enabled the collection of a unique dataset of project-specific outcome

information for empirical research. A careful analysis of the responses was performed by cross comparison of answers to similar or same questions phrased in slightly different ways and presented multiple times in different sections of the survey to ensure the internal validity of responses regarding success. Other responses, such as reporting of publications and patents, were independently validated by information found in external databases.

Research was conducted to identify all publications and patent applications resulting from R&D efforts by a sample of 265 small biotechnology/bioscience firms. How this sample size was reached is explained in the next chapter, which describes the data. Three scientific literature databases were used: PubMed, ISI Web of Knowledge, and Scopus. The databases were compared in a preliminary, feasibility study of publication search success rates in order to determine which database accurately captured all publications or whether all three databases should be utilized.

PubMed is managed by the U.S. National Library of Medicine and primarily includes biomedical citations (over 17 million) from Medline (an online database of 11 million citations and abstracts primarily from health and medical journals) and other life science journals dating back to 1950. Scopus by Elsevier is an abstract and citation database of literature and web sources in all scientific (e.g., chemistry, physics, etc.), technical, medical, and social sciences areas, and it contains 15,000 peer-reviewed journals, over 1000 open access journals, 500 conference proceedings, over 600 trade publications, over 125 book series, 33 million abstracts (16 million records going back to 1996 and 17 million going back as far as 1869), citations from Medline, and 21 million patent records from 3 patent offices: US Patent and Trademark Office (PTO), European

Patent Office, and World Intellectual Patent Office. ISI Web of Knowledge by Thomson™ is a research platform for searching literature in the sciences, social sciences, arts, and humanities, and it contains 9,300 high impact journals with content dating back to 1900, and 4000 of those journals are from biological abstracts with over 9 million records dating back to 1969.

The comparative feasibility study indicated that while PubMed was inadequate in pulling up all publication records, there was almost complete overlap between the search results using ISI Web of Knowledge and Scopus. Therefore, Scopus was chosen to be the primary database accessed for publication and patent search for this dissertation. The database was systematically searched using the firm name (and various acceptable forms of the firm name) to generate a list of all biomedical, scholastic journal articles published by the firms as well as patent applications they had filed.

Once the hit list of publications and patent applications for each firm was generated, the actual papers and patent application documents were retrieved to collect the institutional affiliation information of all co-authors and co-applicants named on the documents. The scientific content of each document was also reviewed and analyzed in order to be able to characterize the type of collaboration and, by extension, help classify and code the type of collaborator/partner. The list of collaborating institutions made up the list of R&D partners that were coded, counted, and subject to various statistical analyses in this dissertation. The count for "partner" was at the institutional level and not at the level of the individual co-authors, so several co-authors from the same institution were counted as one.

Scholars of collaboration have reported encountering methodological problem

with respect to collecting information on university-firm interactions because such interactions are frequently not reported in the business press (McKelvey et al, 2003). On the other hand, there could be concerns that the approach of using academic publications to identify partners might not be valid because of questions about the frequency with which firms publish in academic journals. However, using publications to identify partners was based on prior works found in the alliance literature that employed the same approach (Cockburn & Henderson, 1998). Besides, there is ample evidence indicating that most bioscience firms publish in academic journals regularly, so as to make this approach valid. For example, based on measures comprised of the number of papers published and the number of citations per publication, Genentech and Chiron were on the list of the top 10 most visible scientific institutions in molecular biology from 1988-1992, along with the prestigious research institutions and universities such as the Salk Institute and MIT (Powell et al, 1996). Moreover, citation data collected from 1981 to 1992 showed that the average citations per paper for biotechnology companies (approximately 28 citations) was comparable to the rate for independent and universities labs (approximately 31 citations) (Powell et al, 1996). Collaborative R&D can take place under various types of arrangements, both formal and informal. Irrespective of the types of R&D partnerships involved, scientific peer-reviewed journals serve as a universal venue for members of biomedical research communities, including small and large businesses, to document and disseminate their R&D accomplishments. Unlike many other industries, the culture of the biotechnology industry is such that its members routinely publish and participate in publication practices of the broader bioscience community. Therefore, it has been deemed that co-authorship of scientific papers

between a firm's in-house researchers and scientists from other firms, as well as from academic, government, and non-profit research institutions, can be used as a measure of the extent of networking by a firm.

Statistical Tests

Inferential statistics to test the influence of different types of partners on innovation success involved **logistic regression modeling**, and SPSS statistical software was used. **Analysis of variance (ANOVA)** was performed to determine whether there was a relationship between FDA regulation and the number of clinical partners included in a firm's network of R&D partners. (*This could have also been accomplished by t-test.*)

Cluster analysis of network composition was performed to explore whether firms could be separated into naturally occurring groups based on the network composition patterns. That is, do firms belonging to different bioscience sectors vary in their network composition? Does the network composition pattern differ for firms that succeed in product innovation versus those that do not? Clustering is the partitioning of a set of data points into subgroups or clusters, such that members in a cluster are relatively similar to each other while members of different clusters are relatively dissimilar. In cancer research, for example, clustering is regularly employed in the analysis of gene expression profiles to distinguish different types of tumors. Cluster analysis was performed using an open source R program, which is comprised of an integrated suite of software facilities for data manipulation, calculation, and graphical display. It is available for free in source code form under the terms of the GNU (**G**NU's **N**ot **U**nix) General Public License and can be downloaded from http://cran.r-project.org/bin/windows/base/.

Cluster analyses included 1) unsupervised, hierarchical clustering represented by

dendrograms (also called dendograms) and heat maps, and 2) principal component analysis represented by multi-dimensional scaling plots of the first and second principal components. Hierarchical agglomerative clustering to generate dendrograms involves joining a pair of data points with the smallest distance between them and then, in successive steps, joining pair of clusters that are the closest to each other and forming a new cluster as a result. The distance measures are standard Euclidian in which square root of the sum of squares of the differences are taken: Distance (p,q) = square root $[(p_1-q_1)^2 + \ldots + (p_n-q_n)^2]$, where one of the points is $(p_1,\ldots, p_n)$ and the other point is $(q_1,\ldots,q_n)$. Dendrogram is essentially a one-dimensional ordering of data points, in contrast to the two-dimensional visualization that can be generated by principal component analysis. Each data point could have tens to thousands of components, which means that each point could be represented by tens to thousands (or n number) of dimensions and has the form $(x_1, x_2, \ldots, x_n)$. For example, each "point" could represent a *set* of different types of partners in a network as was the case in this dissertation, or it could represent a set of gene expression values from a tumor sample as another example. A "heat map" is produced when each rectangle representing the *number* of a particular type of partner in a network (or in the cancer research example, representing the *expression level* of a particular gene in a tumor sample) gets color coded. Unsupervised clustering is exploratory and there is no training data taken into consideration, while supervised clustering is performed for the purpose of classification of new data points based on training data.

Pearson's product moment correlation analysis was performed to determine whether there was a relationship between firm age and total number of linkages in a firm's network, as well as number of linkages involving different types of partners.

Variables

All of the variables described in detail in this section are also summarized in Table 2. The unit of observation for all variables was the firm; that is, the variables were firm-specific. The values for outcome measure and firm characteristics were derived from the responses to the SBIR survey questions. Partner typing of each network member was enabled by analyzing the co-authorship data from secondary sources.

Dependent variable

Firm performance is a complex construct and, as discussed previously, a number of different variables can be found in the literature for this outcome measure. They have included financial performance measures as well as various other proxy measures – e.g., patent count (Cockburn & Henderson, 1998; George et al, 2002); number of products on the market (Cyert & Goodman, 1997; Deeds & Hill, 1996; Dowling & Helm, 2006; George et al, 2002; Harmon et al, 1997; Maclachlan, 1995); R&D expenditure (George et al, 2002); net sales to assets, return on equity, net income (George et al, 2002; Rothaermel, 2001); and so on. In this dissertation, logistic regression models have been estimated with innovation outcome as a binary dependent variable (i.e., successful or not successful). Innovation success (**dependent variable INNOV**) was considered to have been achieved when the SBIR product that the firm had been developing successfully made it to the stage of being actually in use by the target population or in the commercialization stage. If the progress fell short of this, e.g., when the product remained under development, innovation was considered to be NOT successful and NOT achieved. **This information was collected from responses to the SBIR survey question, "What**

is the current status of the project funded by the referenced SBIR award?" The survey responders, who were either the principal investigators or other knowledgeable representatives of the firm, had to select only one of from a list of response choices that included "Under development", "Commercialization stage", "In use by target population", "Discontinued", or "Other."

The unit of analysis of innovation success was at the project level (SBIR project level). The unit of analysis of partnership characteristics was at the firm level and for the duration of the time frame in which the firm was working on the SBIR project. It was recognized that some of the partnerships identified would not have been formed specifically for the SBIR-supported project but rather for other products that these small bioscience firms had under development at the same time that they were developing the SBIR-supported product. An important underlying presumption made and indirectly tested in this methodology was the occurrence of knowledge spillovers within the network, although this dissertation did not involve any direct measure of knowledge spillover that would involve tracking the flow of specific knowledge or technology throughout the network to measure the extent of its dissemination and adoption by the network members.

Alliances can carry benefits beyond the specific project for which they were formed and beyond what was specified in a formal agreement as the designated function of the alliance. Hence, knowledge garnered and skills developed from participating in an alliance could have unanticipated benefits not apparent at the outset, in helping advance projects other than just the said project for which the alliance was established. The opportunities to access complementary knowledge through the R&D network established

through various R&D alliances could benefit the SBIR project, even though some of the partners might have been brought into the network for a different project(s). Moreover, knowledge spillovers from R&D alliances could involve acquisition of know-how that is beyond building R&D capabilities and generating scientific discoveries, and can provide opportunities for internalizing other types of know-how, such as those critical for strategic business operations.

Explanatory or independent variables

There are numerous independent variables that could potentially help explain a firm's innovation success. This dissertation research has focused on **network characteristics in terms of the numbers of alliances and the different types of partners comprising the network** as explanatory variables for innovation success. Each R&D collaborator was coded as firm/corporate, university/academic, or clinic, and these three partner types were designated by the variables, **FIRM, UNIV,** and **CLIN**, respectively. Some scholars have used the number of different R&D projects as a measure of the extent of collaboration (Fontana et al, 2006), while others have focused on the total count of strategic alliances (Rothaermel, 2001). Still others have used the number different partners to characterize the extent of a network (Koka & Prescott, 2008). Similarly, this dissertation analyzed the number of linkages or alliances with the above partner types to characterize a firm's R&D network. FIRM**A**, UNIV**A**, and CLIN**A** variables ("A" suffix indicating "alliance") were used to measure the alliance count. Multiple linkages with the same partner on multiple projects or repeated partnerships with the same partner at different times within the time period under study

resulted in higher alliance count. FIRM, CLIN, and UNIV were used as dichotomous variables in the models to denote *the presence or absence* of that partner type in the alliance network. The variable, **NetSize**, represented the size of the network as determined by the total number of alliances with all types of collaborators. The variable to indicate whether the product was subject to FDA regulation was represented by **FDA**. When the SBIR product required FDA approval, it was coded 1, and otherwise coded 0. Finally, in order to determine whether successfully obtaining patents or generating publications from the project was associated with a greater likelihood of a firm's success in innovating, the number of patents and publications generated were included in the models as **Pat** and **Pub** variables, respectively.

Control variables

A firm that has been around longer could be expected to have had more opportunities over the years to establish vertical and horizontal linkages with other firms and to accumulate the necessary skills and experience not only in research and product development but also in business and organizational management as well as alliance management. It was important to ensure that the observed effects were not simply due to age-related performance improvements. Therefore, the analyses performed in this dissertation controlled for any influence of firm **AGE** (i.e., number of years the company has been in existence).

In addition, AGE variable was converted from an integer variable to a dichotomous variable by creating two age groups: start-ups versus older firms. Firms founded less than 4 years prior to the time of SBIR award were defined as "start-up"

(**AgeStartUp** coded as 1), while older firms founded 4 or more years prior to the time of SBIR award were coded as 0. This AgeStartUp variable was used to test the interaction effect between firm age and interfirm alliances on innovation success.

Since larger firms that have greater human capital may be able to accomplish their objectives more quickly and achieve reduced time to market, **firm size** would have been an appropriate control variable to include. However, accurate data on firm size at the time of the SBIR project was unavailable. Although firm size representing the number of employees at the time of survey in 2002 was available, that information could not be used in any predictable way to deduce the number of employees at the time of the SBIR project. Moreover, Powell et al. have shown that firm age had no significance in predicting the firm's growth or central connectedness in the network (Powell et al, 1996). They showed that size was an outcome rather than a predictor of network behavior and partnering.

Classification of partners

After the collaborators/partners were identified and their "affiliation" data collected from Scopus search results, they were first classified into 3 categories: 1) firm/corporate, 2) university/academic, and 3) clinic. This section describes in greater detail the criteria that were used to place the firms into these different categories. The terms "firm", "industry", and "corporate" are used synonymously throughout this dissertation when referring to R&D partners. Also, "university", "academic", and "basic" are used synonymously.

Clinical partners

Leading research universities are frequently affiliated with teaching hospitals and medical centers. Conversely, medical schools, pharmacy schools, and dental schools are part of universities, and it is possible to classify them as either "clinic" or "academic." Medical research is not necessarily clinical research, and biomedical research can, in fact, be very basic and mechanistic in nature. For all of these reasons that complicate classification, it was important to clearly outline the criteria for distinguishing between a university partner from a clinic partner.

The main criterion was that the predominant function of an organization classified as "clinic" involve providing clinical services to patients, and each partner was analyzed to determine whether it satisfied this. Accordingly, hospitals, clinics, clinical centers, medical centers, community health centers, health maintenance organizations, and *Comprehensive* Cancer Centers, were always classified as **CLIN**. It should be noted that not all NCI-designated Cancer Centers are Comprehensive Cancer Centers and they are not all clinical (e.g., Wistar Institute is not). Sidney Kimmel Cancer Center (San Diego), despite its name, is not a Comprehensive Cancer Center and was classified as academic/basic because it is primarily a non-profit research organization that does not contain a clinic. Despite the similarity in name, there was no confusion in classifying Kimmel Cancer Center (Philadelphia), which **is** a Comprehensive Cancer Center that provides clinical care, as "clinic". Organ banks were grouped under "clinic."

In the case of a medical school partner, it was coded as either **CLIN** or **UNIV**, upon further analysis of the departmental/division affiliation as well as an analysis of the nature of research that was conducted. It was classified as CLIN when a clinical

department or discipline was specified in the affiliation. If no department was designated, scientific content of the paper was analyzed. Generally speaking, areas of study that are patient-oriented, applied, and highly translational were considered clinical. For example, department of surgery or department of radiology would be classified as CLIN because the practice of surgery or radiology is inherently clinical in nature and not basic. Radiobiology, on the other hand, would be basic and the medical school would then be coded as UNIV. Obviously, whenever the term "clinical" appeared as part of the name of a department or division, that partner was classified as clinical. The specific disciplines that were classified as "basic" and those classified as "clinical" are listed in Appendix B.

University/basic partners

University/basic partners included not only universities, but also non-profit research organizations and government laboratories. In the area of bioscience, the function of government laboratories is generally the same as that of university-based research laboratories, and their focus is predominantly on basic research. However, government research partners affiliated with a government hospital or clinic (e.g., National Naval Medical Center, NIH Clinical Center) could be conducting research that is more translational and clinical in nature, in which case those partners would be classified as "clinical."

Further classification of firm/corporate partners

Firm partners were further classified based on their size and their area of specialty. Firm partners were classified as being a big firm (**BigFirm**) when they had over 1000 employees, and this variable was tested to see if partnering with a large firm(s) might have a positive effect on innovation (hypothesis 2), which might not be observed in the absence of making this distinction in corporate partner characteristics.

Firm partners were also classified into the following six categories: pharmaceutical, biotechnology, diagnostic, CRO/service, research tools, and other. Information needed to accurately classify the companies were researched and obtained from 1) self-description on company websites, 2) company profile in publicly available, online industry directories, and 3) analysis and characterization of firm's portfolio of products. The following industry databases and directories available online were used: Conde Nast Portfolio (http://www.portfolio.com/resources/company-profiles); and Manta (http://www.manta.com).

Drawing the line between different categories can be difficult to do and somewhat subjective. To guard against this, detailed criteria for placing firms into the categories were established and consistently applied. The criteria are described here. "**Pharmaceutical"** firms were those that develop and sell small molecule (i.e., chemical) drugs as their major product line. Biopharmaceutical companies developing biodrugs were classified as "**biotechnology"** as opposed to **pharmaceutical**. Biodrugs or biologics include therapies that are biological in nature or derived from biological sources, as distinct from the traditional chemical drugs/pharmaceuticals. They include gene therapies, RNA-based (e.g., RNAi and antisense) therapies, immunotherapies (i.e.,

therapies involving antibodies or immune cells), stem cell-based therapies, ribozymes as therapeutics, proteins and peptides as therapeutics, and even vaccines. Biotechnology is an integral component of biodrugs, or an integral component in the development or synthesis of biologics. Firms involved in proteomics research or in developing nanotechnologies were also grouped under "biotechnology." It is important to recognize many biotechnology firms frequently include the word "pharmaceutical" in their company name, which can be quite misleading and makes product analysis of such companies important.

"Diagnostics" firms included those associated with in vitro diagnostics, molecular diagnostics, and clinical chemistry diagnostics. Established manufacturers of large in vivo diagnostics equipment were not included in this category, but rather in the "other" category described below. **"CRO/services"** included both contract research organizations that specialize in providing laboratory and pre-clinical research services, as well as clinical research organizations that specialize in the management of clinical trials. CRO/services category also included other service firms, such as medical laboratory service providers (e.g., pathology laboratory, virus laboratory), consulting firms, and contract manufacturers. Firm were classified under **"research tools"** when they produce reagents used in research or components of assays and kits (e.g., fluorescent enzyme substrates, oligonucleotides, plasmids), platform technologies (e.g., microarrays and microfluidics technologies) and other laboratory devices (e.g., cell plates). They also included firms that generate transgenic mice for use as models. **"Other"** category included firms producing medical devices (e.g., implants), instrumentation, electronics, equipment, software, bioinformatics tools, assessment tools (non-research), healthcare

consumer products (e.g., contact lenses, cosmetics, needles and syringes), chemicals (non-drug), and materials. Although hospital equipment for X-ray, ultrasound, and MRI are used for diagnostic purposes, manufacturers of such equipment were grouped under "other," because such companies do not conduct diagnostics research per se.

Table 2. Description of variables.

Variable	Definition
INNOV	Innovation success (binary variable) Yes = Product is currently in use by target population or in the commercialization stage (code=1) No = Product is still under development (code=0)
AGE	Age of firm at time of SBIR award (year award made minus year company founded) (integer/count variable)
AgeStartUp	Is the firm young or old (binary variable) Young firms founded less than 4 years prior to the year of SBIR award (i.e., start-up) (**code=1**) Older firms founded 4 or more years prior to the year of SBIR award (code=0) This variable was used to have the older firms be the reference group
AgeStartUpR	Is the firm young or old (binary variable) Young firms founded less than 4 years prior to the year of SBIR award (i.e., start-up) (**code=0**) Older firms founded 4 or more years prior to the year of SBIR award (code=1) This variable was used to have the start-ups be the reference group.
NetSize	Total number of all partners, including all different types of partners, within the network (integer/count variable)
UNIV	Presence or absence of a university partner in the network (binary variable) There is at least 1 university partner (code=1) No university partner (code=0)
UNIVA	Number of alliances with university partners, including repeated or multiple alliances with the same university partner (integer/count variable)
FIRM	Presence or absence of a firm partner in the network (binary variable) There is at least 1 firm partner (code=1) No firm partner (code=0)
FIRMA	Number of alliances with firm partners, including repeated or multiple alliances with the same firm partner (integer/count variable)

Table 2. Description of variables (continued).

BigFirm	Presence or absence of a large corporate partner that has over 1000 employees (binary variable) There is at least 1 big firm partner (code=1) No big firm partner (code=0)
BigFirmA	Number of alliances with large corporate partners/collaborators within the network (integer/count variable)
CLIN	Presence or absence of a clinical partner in the network (binary variable) There is at least 1 clinical partner (code=1) No clinical partner (code=0)
CLINA	Total number of alliances with clinical partners, including repeated or multiple alliances with the same clinical partner (integer/count variable)
FDA	FDA approval (binary variable) Yes = Product requires FDA approval required (code = 1) No = Product does not require FDA approval (code = 0)
PatYN	Success in patenting (binary variable) Yes = Patent application(s) files or patent(s) obtained (code = 1) No = No patent obtained or application filed (code = 0)
Pat	Number of patent applications filed and patents obtained (associated with the SBIR-supported product/project) (Integer/count variable)
PubYN	Success in publication (binary variable) Yes = Publication(s) generated (code = 1) No = No publication generated (code = 0)
Pub	Number of publications (associated with the SBIR-supported product/project) (Integer/count variable)

Note: The product/project refers to the specific product/project whose development was supported by SBIR.

Model Specification

Hypotheses regarding the effects of explanatory variables and the influence of predictors on innovation success were tested using logistic regression analyses, where *p*(INNOV) represented the predicted probability of innovation success, and 1-*p*(INNOV) represented the predicted probability of **no success** in innovation. First, a baseline model (Model 1) containing AGE as the only independent variable was tested before expanding the logit model to include other variables. In Model 2, the variable *NetSize* was added to the baseline model to test whether the overall R&D network size was associated with greater likelihood of innovation success. This served as the reference. **Network size (NetSize) was defined as the total number of direct R&D partners with whom the firm had collaborated** during the 6 years *nesting the SBIR project (i.e., encompassing the entire SBIR project period plus a few post-SBIR years)*.

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1 \text{AGE} \quad \textbf{(Model 1)}$$

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1 \text{NetSize} + \beta_2 \text{AGE} \quad \textbf{(Model 2)}$$

In order to estimate the influence that specific types of alliance partners might have on innovation success, NetSize was replaced by the **dummy variables** representing firm/industry partners (FIRM), clinical/hospital partners (CLIN), and university/basic laboratory partners (UNIV) in **Model 3A**. That is, FIRM, CLIN, and UNIV variables were used to determine whether having these types of partners versus not having them within the network had an effect on innovation success. In **Model 3B**, innovation was modeled as a function of alternative measures to characterize the R&D network, namely

variables representing the **number of** alliances with firm partners (FIRMA), **number of** alliances with clinical partners (CLINA), and **number of** alliances with university partners (UNIVA).

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1 \text{AGE} + \beta_2 \text{FIRM} + \beta_3 \text{CLIN} + \beta_4 \text{UNIV}$$

(Model 3A)

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1 \text{AGE} + \beta_2 \text{FIRMA} + \beta_3 \text{CLINA} + \beta_4 \text{UNIVA}$$

(Model 3B)

Models 4A and 4B were used to test the hypothesis that for young (i.e., start-up) bioscience firms, interfirm alliances are positively associated with innovation success. This relationship may not necessarily hold for older firms. That is, having alliances with other firms may be more important for *young start-up* firms than for older firms. Similarly, alliances with other types of partners such as firm-university alliances may not have the same kind of effect that firm-firm alliances do. Model 4A served as a baseline model without the interaction terms, and Models 4B and 4C were used to test for interaction effects between firm age and interfirm linkages and between firm age and firm-university linkages, respectively.

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1 \text{AgeStartUp} + \beta_2 \text{FIRMA} + \beta_3 \text{CLINA} + \beta_4 \text{UNIVA}$$

(Model 4A)

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1\,\text{AgeStartUp} + \beta_2\,\text{FIRMA} + \beta_3\,\text{CLINA} + \beta_4\,\text{UNIVA} + \beta_5\,\text{AgeStartUp*FIRMA}$$ **(Model 4B)**

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1\,\text{AgeStartUp} + \beta_2\,\text{FIRMA} + \beta_3\,\text{CLINA} + \beta_4\,\text{UNIVA} + \beta_5\,\text{AgeStartUp*UNIVA}$$ **(Model 4C)**

Models 5A and 5Bwere used to test the hypothesis that having big firms in the R&D network is associated with innovation success. The dummy variable **BigFirm,** representing the presence or absence of a large corporate partner in the network, was used in Model 6A to test whether having at least one big firm as an R&D partner was important. BigFirmA in model 5B represented the total number of alliances with large firm partners in the network. **Big Firms were defined as companies with over 1000 employees.**

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1\,\text{AGE} + \beta_2\,\text{BigFirm} + \beta_3\,\text{CLIN} + \beta_4\,\text{UNIV}$$ **(Model 5A)**

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1\,\text{AGE} + \beta_2\,\text{BigFirmA} + \beta_3\,\text{CLINA} + \beta_4\,\text{UNIVA}$$ **(Model 5B)**

Model 6A included the **FDA** variable (i.e., whether or not FDA approval was needed) to assess the impact of FDA regulation on innovation success. Model 6B containing the CLINA*FDA interaction term was used to test the hypothesis that firms

developing FDA-regulated products are more likely to succeed in product commercialization and innovation when they have a greater number of alliances with clinical partners (e.g., hospitals, clinics, clinical centers, medical centers).

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1 \text{AGE} + \beta_2 \text{FIRM} + \beta_3 \text{CLIN} + \beta_4 \text{UNIV} + \beta_5 \text{FDA}$$

(Model 6A)

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1 \text{AGE} + \beta_2 \text{FIRM} + \beta_3 \text{CLIN} + \beta_4 \text{UNIV} + \beta_5 \text{FDA} + \beta_6 \text{CLIN*FDA}$$

(Model 6B)

Model 7A contained dichotomous predictor variables PatYN and PubYN for "yes" or "no" on whether any patents or publications were generated from the SBIR project, respectively; and model 7B contained integral variables, Pat and Pub, representing the total number of patents and publications generated from the SBIR project, respectively. These models were used to test whether these patent and publication output measures could predict innovation outcome, as there are no guarantees that ideas that are published or patented will be successfully developed and materialize into commercialized products. (Chi-square test for independence could have also been performed to obtain the same information on whether there is a relationship between success in generating publication(s) and innovation success; and between success in obtaining patent(s) and innovation success.)

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1 \text{FDA} + \beta_2 \text{PatYN} + \beta_3 \text{PubYN}$$

(Model 7A)

$$\ln[p(\text{INNOV})/1\text{-}p(\text{INNOV})] = \beta_0 + \beta_1 \text{FDA} + \beta_2 \text{Pat} + \beta_3 \text{Pub}$$

(Model 7B)

CHAPTER 7: DATA AND RESULTS

Overview of Data Analyses Performed

This chapter begins with descriptive **summary of the characteristics of SBIR-funded firms and projects**, and includes contingency **tables showing firms and projects grouped into various categories**. It reports on some general characteristics of the types of firms that the NIH SBIR program has supported. The analyses of partnership data include examining network characteristics in terms of both the types of partners and also their numbers and proportions that make up the network composition. The results from subjecting the partnership/alliance data to multiple inferential statistical analyses are presented later in the chapter.

Inferential statistics were performed to address specific hypotheses posed in this dissertation regarding the effects of R&D partnering activities on the innovation performance of firms. That is, the significance of network characteristics in terms of the types of partners and the number of alliances as predictors of innovation success was assessed. Also, product attribute with respect to whether it was FDA-regulated was a focus of analysis to determine whether it moderated the impact of R&D partnering on innovation success. Finally, the relationship between short-term outputs (i.e., patents and publications resulting from the project) and long-term outcomes (commercialization/innovation success) was examined to determine whether such output measures of short-term productivity could serve as surrogate measures for successful outcome.

SBIR Survey Data Analysis

The SBIR Program evaluation involved surveying the firms that received NIH SBIR Phase II grants between 1992-2001, and there were 768 respondents (86% response rate) (NIH, 2003). Out of the 768 firms that responded to the survey, this dissertation research focused on the 265 firms that engaged in the development of high-technology products and self-classified their major field of business as "biotechnology", "pharmaceuticals", or "diagnostics" in response to the **survey question: "Which of the following best describes this company's major field of business?"** Firms producing educational materials and health information materials for educators and the general public, or firms developing products for mental health or drug abuse-related uses, for example, were not included in the sample, as such products were not high-technology nor R&D-intensive.

Firm characteristics

Table 3 shows the characteristics of the 265 ***"small" (according to the Small Business Administration (SBA) definition*) firms that received SBIR funding from the NIH**. It shows that 169 firms classified themselves as a biotechnology firm, 54 classified themselves as a pharmaceutical firm, and 42 described themselves as a diagnostic firm.

The majority of firms in all three categories had 50 or fewer employees. In fact, 35% of biotechnology, 44% of pharmaceuticals, and 50% of diagnostics firms were **very small businesses with fewer than 10 employees. However, this information on firm size should be regarded as just a rough gauge of the size of firms supported by SBIR funding** because the survey responders had recorded the size of the firm *at the time of the*

survey in 2002, which could have been many years post-award. The responders were not instructed to recall the firm size at the time that the award was made. This can explain why there were firms recorded as having greater than 500 employees even though all companies had to have fewer than 500 employees to be defined as "small" and be eligible for SBIR funding.

This also raised the question of whether incorporating "firm size" as a variable in the analyses would be valid, as the data collected did not **accurately** reflect the *values at the time of award*. Therefore, size was not included in the analyses, even though it would have been useful to include size in the baseline model to see if it had an effect on innovation success. On the other hand, since all of the companies were officially designated as small firms to begin with, any interesting findings generated from a further breakdown into different groups of smallness would have been limited in its generalizability (i.e., not generalizable to large firms).

Instead, the research questions and hypotheses in this dissertation focused on firm age and the differences between start-up versus older firms. Firm age (i.e., number of years the firm has been in existence) was the age at the time of the SBIR award, not at the time of the survey. This was calculated by subtracting the year that the firm had been founded from the year that the SBIR award was made. The SBIR-funded firms were well distributed across all years as shown in Table 3. Although almost all start-ups and very young firms can be expected to be small, not all small firms are young. Table 3 shows that nearly one quarter of all firms (24% of biotechnology, 24% of pharmaceutical, 24% of diagnostics) taking advantage of the SBIR program had been around for over a decade.

Table 3. Characteristics of SBIR-funded small businesses.

	Biotechnology	Pharmaceutical	Diagnostics
N (total number of firms)	169	54	42
Firm size (number of employees)[1]			
Fewer than 10	59	24	21
10-50	64	17	9
51-100	16	5	3
101-500	21	6	5
501-1000	3	1	3
Great than 1000	6	1	1
Firm age (years)[2]			
Less than 5	50	18	13
5-10	78	24 [3]	19
Over 10	41	13	10

[1] Firms size was the number of employees *at the time of the survey in 2002*. The survey responders provided the current figures at the time of the survey in 2002; and several firms have grown in size since first participating in the SBIR program, which restricts eligible firm size to 500 employees.

[2] Firm age was the value at the time of the SBIR award (i.e., the number of years the firm has been in existence at the time of the award), not as of the year of the survey.

[3] A firm was counted twice because it had received two SBIR grants in two different years.

Project characteristics

This section describes the results from focusing the survey data analysis on the 266 *projects*, as opposed to the firms. Table 4 is a cross tabulation (or contingency table) showing count data for the number of projects that fell under various categories of product type, novelty of product, and outcome in terms of commercialization/innovation success. **Product type** categories were based on responses to the **survey question, "…what product, process, or service did you plan to commercialize?"** and included the following: drug, biologic, diagnostic, research tool, genomic, and other. "Biologic" frequently refers to "biodrug" and includes therapies that are biological in nature, such as gene therapies, RNA-based (e.g., RNAi and anti-sense) therapies, immunotherapies (i.e., therapies involving antibodies or immune cells), stem cell-based therapies, ribozymes as therapeutics, proteins and peptides as therapeutics, and vaccines. Data on product novelty were obtained from responses to the **survey question, " Which one of the following most characterizes the product, process, or service that was planned under this project?"** where following five answers were available for selection: a totally new product, process, or service; an improvement to an existing product, process, or service; a combination of products, processes, or services; a new use for an existing product, process, or service; and other. Finally, innovation was determined to have been successful for the purposes of this dissertation research when either "commercialization stage" or "in use by target population" was selected as the response to **the survey question, "What is the current status of the project funded by the referenced SBIR award?"** All other responses for project status, which indicated or implied less progress, were coded as "no" innovation success.

Table 4. Characteristics of SBIR-funded projects.

	Product Type					Total
	Drug	**Biologic**	**Diagnostic**	**Research tool, genomic**	**Other**	
N (number of projects)	74	43	19	57	73	266
Degree of novelty						
Totally new product	56	32	16	43	49	196
Improvement to, new use for, or combination of existing product(s)	18	11	3	14	24	70
Status of project						
Under development	50	27	5	12	30	124
Commercialization stage	6	6	6	16	17	51
In use by target population	0	4	3	19	20	46
Discontinued	18	6	5	10	6	45
FDA regulated	67	29	10	3	39	148

A notable observation was that diagnostics made up a very small fraction (less than 10%) of products supported by SBIR funding. The majority (74%) of projects involved high degree of novelty, involving the development of a totally new product. Over one-half (56%) of products required FDA approval, and slightly less than one-half (47%) of products failed to reach the commercialization stage. The data appeared to support a generalization well-acknowledged by the scholars of this industry that having to

obtain regulatory approval significantly increases the development time and poses a major hurdle in the successful commercialization of products (Booth et al, 2003; Coplan et al, 2004). For instance, over 90% of drugs in this study required FDA approval and none has yet made it to use by the target population. Almost 70% of the 43 biologics required FDA approval and there were less than 10% (only 4 products) in use by the target population. On the other hand, less than 20% of the 57 research tools and genomic technologies required FDA approval and one-third (19 products) were already in use by the target population. The majority of commercialization successes achieved were by firms working on products that did not require FDA approval, such as tools and software. In summary, research tools had a much greater success rate than pharmaceuticals.

Characteristics of diagnostics-related firms and products

Diagnostics-related projects and diagnostic firms were a focus of analysis in this dissertation for a number of reasons. First, this is a small bioscience sector that has been underserved by the NIH; yet its potential to have tremendous clinical relevance is now greater than ever before. Diagnostics is poised to become a central player in shaping the future success of personalized medicine, and policies to foster the growth in this area of bioscience are needed. In order to create new programs or initiatives for this sector, it would be helpful to have some understanding of the level of activity of diagnostics firms in pursuing and attaining federal R&D support through programs such as the NIH SBIR Program, and their activities in interacting and forming alliances with pharmaceutical and biotechnology firms. Thus far, not much research on the alliance behavior of diagnostics firms has been conducted and reported in the literature. Table 5 shows a break down of

the types of firms that produce these diagnostics-related (i.e., functionally diagnostic) products, as well as a break down of the types of products that these diagnostics-related products were classified under. The results show that only about 50% of diagnostics-related products were developed by dedicated diagnostics firms, and the remaining 50% by biotechnology firms. Of the 41 diagnostics-related products, 34% (14 products) were identified as devices, assessment tools, software, and other. A discussion of the partnering behavior of diagnostics firms is presented later in this chapter.

Table 5. Types of firms that produce diagnostics-related products.

<table>
<tr><td rowspan="2"></td><td colspan="5">Firm Type</td><td rowspan="2">Total</td></tr>
<tr><td colspan="2">Biotechnology</td><td>Pharmaceutical</td><td colspan="2">Diagnostics</td></tr>
<tr><td>Diagnostic products</td><td colspan="2">8</td><td>2</td><td colspan="2">9</td><td>19</td></tr>
<tr><td rowspan="4">Diagnostics-related (i.e., functionally diagnostic) products</td><td colspan="2">19</td><td>3</td><td colspan="2">19</td><td rowspan="4">41</td></tr>
<tr><td colspan="5">Product Type</td></tr>
<tr><td>Drug</td><td>Device, Chemical, Assessment Tool, Software, Other</td><td>Biologic</td><td>Genomic, Research Tool</td><td>Diagnostic</td></tr>
<tr><td>0</td><td>14</td><td>3</td><td>5</td><td>19</td></tr>
</table>

Partnership and Network Data Analyses

Using the Scopus database described in Chapter 6 to perform literature and patent searches, 6,848 scientific publications and 10,489 patents/patent applications were

identified as having been generated by the 265 firms during a 6-year period starting from the year that the SBIR award was made and extending forward in timeline. The entire duration of the SBIR project period was included in this time frame. These were reviewed and analyzed to generate the data on the network of partners. 3174 partnerships were identified, and information on the partners was researched and analyzed to place them into the following three categories: university/basic; firm/corporate; and clinic. The precise criteria used in the classification were described in Chapter 6.

Partnership characteristics

Table 6 shows a breakdown of ***firm count*** according the number of linkages formed with different types of R&D partners. It also shows the count of firms belong to different bioscience subsectors. On average, a firm in the biotechnology sector had approximately 6 ties with universities, 4 ties with clinical partners, and 3 ties with other firms during the 6-year period. A firm in the pharmaceutical sector had on average 5 ties with universities, 4 ties with clinical partners, and 3 ties with other firms. A firm in the diagnostic sector had 3 ties with universities, 4 ties with clinical partners, and 1 tie with other firms. These values were derived by dividing the number ties/linkages with respective partners (i.e., total number of linkages for all biotechnology firms or all pharmaceutical firms or all diagnostic firms shown in Table 7) by the total number of biotechnology firms or pharmaceutical firms or diagnostic firms in the sample (presented in Table 6). The values were rounded up to whole numbers. The most obvious trend observed here was that diagnostics firms were by far the least likely to engage in R&D collaborations with other firms. Almost 50% of diagnostics firms had no linkages with

other firms. The behavior of biotechnology and pharmaceutical firms with respect to the number of linkages they formed with different types of partners was similar and comparable. Both biotechnology and pharmaceutical firms had the greatest number of linkages with basic/academic research institutions (i.e., universities, federal laboratories, and non-profit research institutes) over the other types of partners, with greater than 75% of biotechnology and pharmaceutical firms having one or more linkages with academic or basic research institutions.

Table 6. Number and proportion of firms grouped according to their linkages with various types of R&D partners.

		Biotechnology	**Pharmaceutical**	**Diagnostics**
Total number of firms		169	55	42
Number of firms with clinic linkage(s)	0 linkages	61 (36%)	20 (36%)	20 (48%)
	1-5 linkages	68 (40%)	25 (45%)	13 (31%)
	6-10 linkages	22 (13%)	6 (11%)	4 (10%)
	Over 10 linkages	18 (11%)	4 (7)	5 (12%)
Number of firms with university/basic linkage(s)	0 linkages	41 (24%)	12 (22%)	14 (33%)
	1-5 linkages	65 (38%)	24 (44%)	21 (50%)
	6-10 linkages	36 (21%)	14 (25%)	3 (7%)
	Over 10 linkages	27 (16%)	5 (9%)	4(10%)
Number of firms with firm linkage(s)	0 linkages	64 (38%)	22 (40%)	20 (48%)
	1-5 linkages	81 (48%)	26 (47%)	21 (50%)
	6-10 linkages	15 (9%)	4 (7%)	1 (2%)
	Over 10 linkages	9 (5%)	3 (5%)	0 (0%)

Table 7 displays the ***number of R&D linkages*** formed by firms comprising the three bioscience subsectors of interest (i.e., biotechnology, pharmaceutical, and diagnostics). Interfirm linkages were further grouped into categories based on the type of partner firm. Specific details on the criteria used to classify the firms were described in Chapter 6. It is shown in Table 7 that **biotechnology firms tended to form alliances with other biotechnology firms, while pharmaceutical firms tended to form alliances with other pharmaceutical firms. However, CROs and service providers comprised the greatest proportion of firms with which the diagnostics firms formed R&D partnerships.** In fact, one-third of the linkages formed by the SBIR diagnostics firms were with CROs and service providers.

The data in this table support the previous observation that diagnostics firms engaged in R&D collaborations only sparsely. While the data in Table 6 represented the propensity of the SBIR firms to form R&D collaborations, the data in Table 7 focused on the partners of these SBIR grantees. Diagnostic firms made up only approximately 5% of the firms with which the SBIR grantees engaged in R&D partnerships.

Table 7. Total number of linkages with different types of R&D partners.

		SBIR Firms		
		Biotechnology	**Pharmaceutical**	**Diagnostics**
Total number of linkages		2172	627	377
Number of firm-university/basic linkages		960	270	141
Number of firm-clinic linkages		747	219	176
Number of interfirm linkages	Pharmaceutical	118	51	7
	Biotechnology	178	37	15
	Diagnostics	17	5	6
	CRO/service	51	19	19
	Research Tools	31	8	3
	Other	70	19	10
	Total	465	138	60

Cluster analysis of network characteristics

Cluster analysis was performed to see whether the SBIR firms would form natural groupings based on the patterns of the R&D partnerships they have formed, i.e., the overall composite of the different numbers and types of partners formed by each firm. This would be one approach for analyzing the patterns of R&D network composition to characterize the firms. For instance, does the mix of academic and industry partners that biotechnology firms interact with differ in some recognizable or definable way from that of diagnostics firms? The results of clustering were visualized using two different methods: dendrograms and multi-dimensional scaling (MDS) plots.

Figure 2 shows dendrograms of cluster analyses examining whether the combination of the different types of partners in a firm's R&D alliance network could lead to natural groupings that could distinguish different types of SBIR-supported firms or distinguish the SBIR-supported firms that are successful in innovation from those that are not successful. **There were no obvious clusters in either analysis**, indicating that there was no pattern to the combination of basic (both academic and federal laboratory), industry, and clinic collaborators that was particularly characteristic of biotechnology, pharmaceutical, and diagnostic sectors, nor could characterize the successful firms from those that were not.

Figure 2. Dendrograms of cluster analyses of partnership pattern based on R&D partner type.

Legend for dendrogram by project success:

Yellow=Under development
Blue=Commercialization stage
Red=In use by target population
White=Discontinued

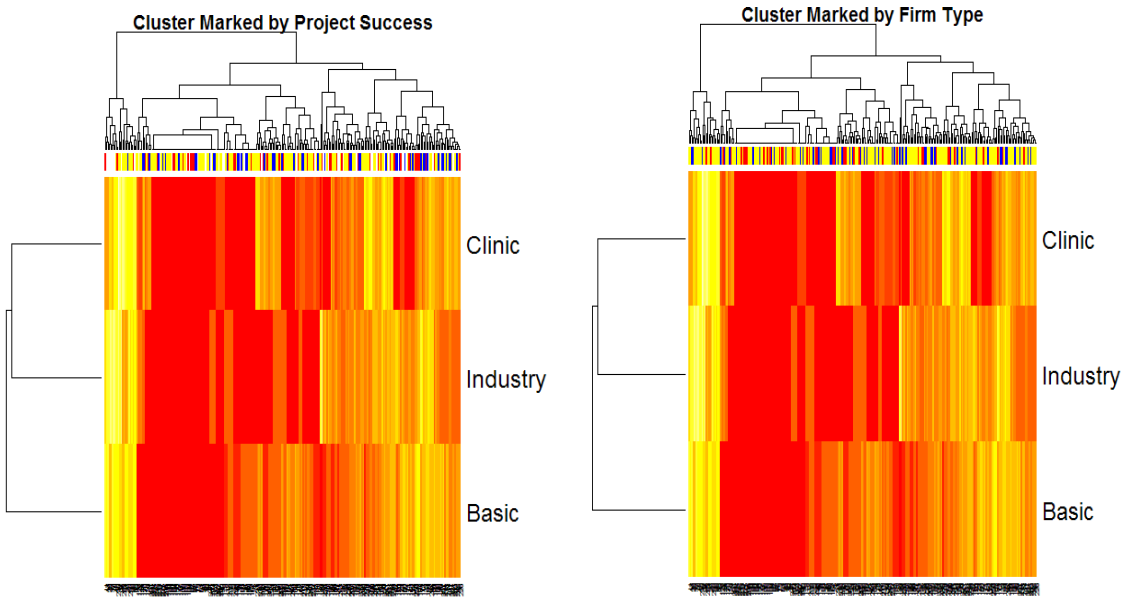
Legend for dendrogram by firm type:

Yellow=Biotechnology firms
Blue=Pharmaceutical firms
Red=Diagnostics firms.

Number of linkages is indicated by color spectrum ranging from darker colors to lighter colors:

Darker colors (e.g., dark red) = fewer linkages
Lighter colors (e.g., light yellow) = more linkages

Interpretations: When the colored bars at the top row representing different types of firms or different levels of project success are clustered, then the data are meaningful.

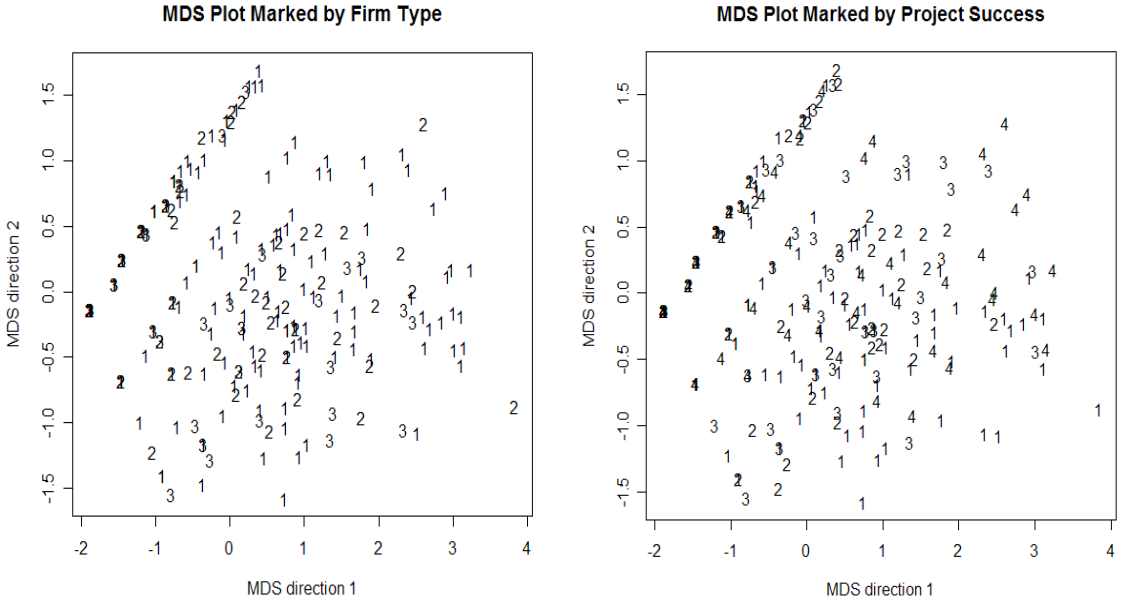


MDS plots in Figure 3 confirmed the same lack of natural clustering. These plots are actually a two-dimensional collapse of three-dimensional data (representing clinic, industry, and basic).

Figure 3. MDS plots of cluster analyses of partnership pattern based on R&D partner type.

Legend for plot by firm type:
1=Biotechnology firms
2=Pharmaceutical firms
3=Diagnostics firms

Legend for plot by project success:
1=Under development
2=Commercialization stage
3=In use by target population
4=Discontinued



Cluster analysis shown in Figure 4 examined whether grouping can occur according to product type (i.e., type of product resulting from the SBIR project). Again, this resulted in no definitive clusters, although firms producing devices, chemicals, assessment tools, and softwares (represented by blue lines) somewhat tended to be aggregated together, characterized by sparse partnerships with very few (represented by dark red shades) clinic, industry, and basic partners in the firm's network. That is, firms developing such product types tended not to form dense alliance networks with other research or corporate entities.

Relationship between firm age and network size

In order to determine whether there was a relationship between firm age and total number of alliances in a firm's network, correlation analysis was performed and the results are shown in Table 8. No correlation between firm age and the overall network size was observed, and there was no correlation between firm age and the number of alliances for all partner categories, including big firms. **Figure 5 depicts graphically the lack of correlation between these variables.**

Figure 4. Dendrograms of cluster analyses of partnership pattern based on product type.

Product type: Yellow=Drug; Blue= Device, chemical, assessment tool, software, other; Red=Biologic; Green=Research tool, genomic; White=Diagnostic.

Number of linkages: color spectrum ranging from darker colors (fewer linkages) to lighter colors (more linkages)

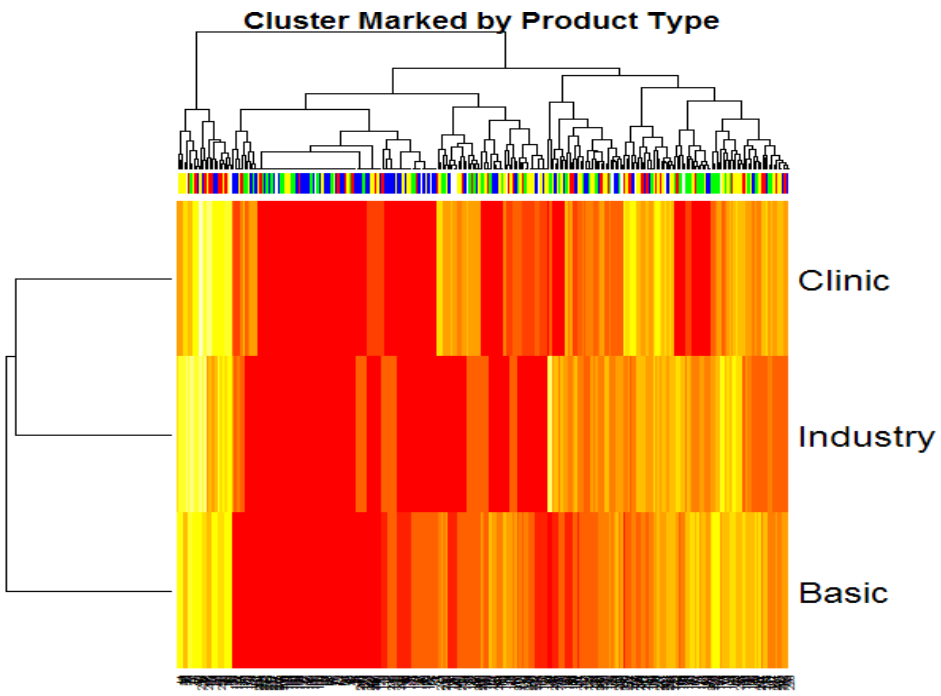
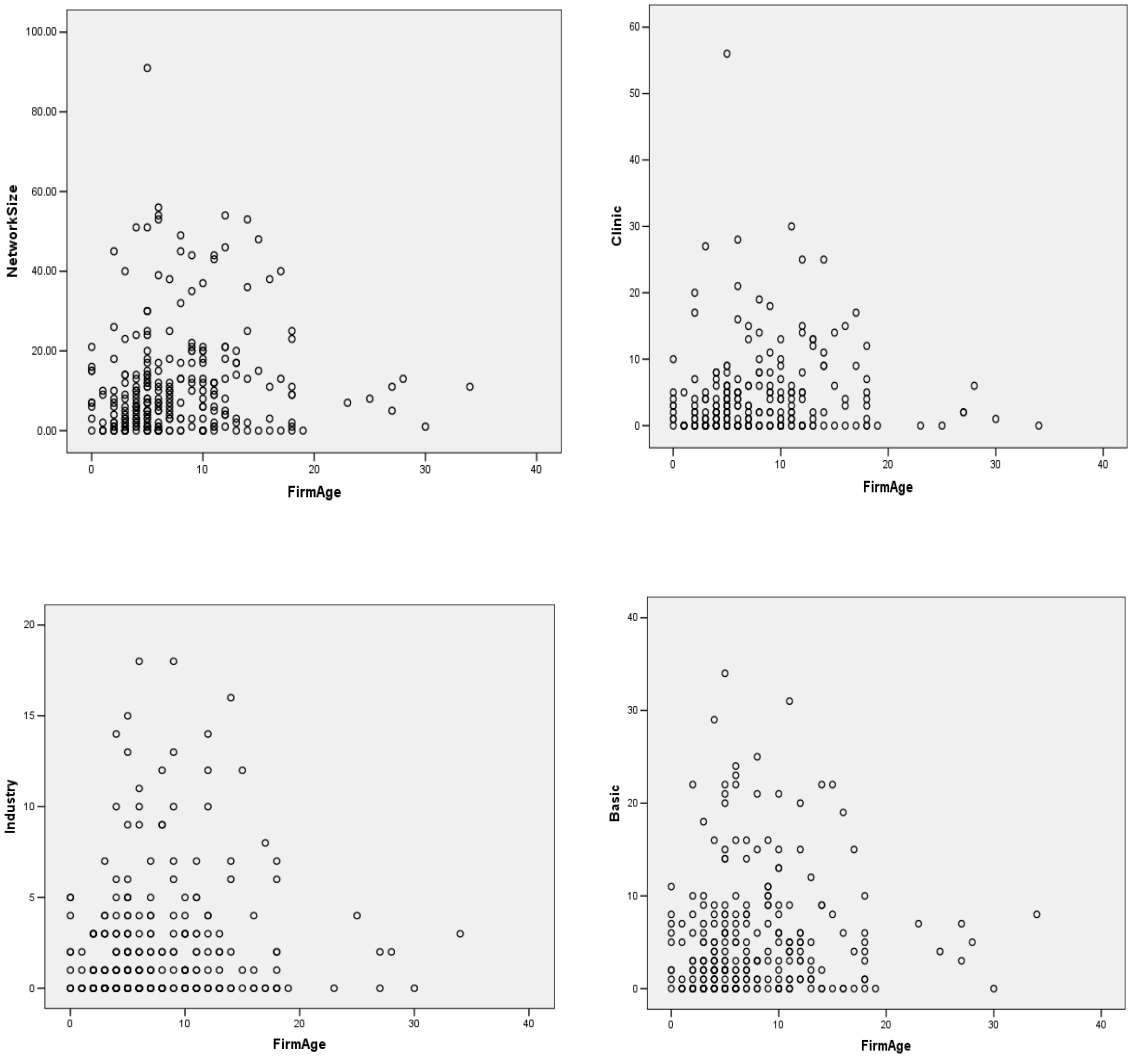


Table 8. Pearson correlation between firm age and number of R&D partners.

		Network size	Basic/ University	Industry	Clinic	Big firm
Firm age	Pearson Correlation	.094	.064	.075	.098	.044
	Sig. (2-tailed)	.126	.295	.220	.111	.473
	N	266	266	266	266	266

Figure 5. Scatter plots of the relationship between firm age and number of R&D partners.

R&D partners are shown for following categories: Basic/University, Clinic, Industry. Network size refers to the total of all different types of partners.



Regression Analysis of Determinants of Innovation Success

Logistic regression models were tested to analyze the effects of various factors pertaining to network and firm characteristics on the innovation outcome of the SBIR projects.

Network size

It has been theorized that the competence and capacity of a firm to innovate are enabled by the extent of its networking (Powell et al, 1996). Hence, a larger network with greater number of alliances would be expected to have a positive impact on the likelihood of innovation success. In order to determine whether the overall network size affects innovation success, logistic regression Model 2 was tested. Model 1 with AGE as the only independent variable served as the baseline. The estimates presented in Table 9 show that the overall network size, which represents the total number of alliances with all types partners within the R&D network, was not a significant determinant of innovation success.

Table 9. Results of logistic regression analysis of network size as a determinant of innovation success.

Dependent variable is INNOV, where innovation success includes having the product currently in use by target population or in the commercialization stage.

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	.010	.025	.168	1	.682	1.010
	Constant	-.323	.232	1.934	1	.164	.724

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	302.896	.001	.001

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	.010	.025	.167	1	.683	1.010
	NetSize	.000	.010	.000	1	.992	1.000
	Constant	-.322	.248	1.677	1	.195	.725

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	302.896	.001	.001

Types of R&D partners and alliances

Models 3A and 3B **(**specified in Chapter 6**)** were used to test whether the inclusion of particular types of partners and the number of alliances with those partners in the network had any influence on innovation success. Firm age (AGE) was included as a control variable, although this may not have been really necessary since AGE along with NetSize had already been shown to not have a significant impact on innovation. The results from testing these models are presented in Table 10, and the data show that R&D alliances characterized according to partner type did not have an impact on innovation, except for clinic partners. An increase in the number of alliances with clinic partners was associated with a decreased likelihood of innovation success, and an explanation for this unexpected trend is provided later in this chapter when the impact of FDA regulation as an explanatory variable is discussed.

Table 10. Results of logistic regression analysis of alliances with different types of partners as determinant of innovation success.

Dependent variable is INNOV, where innovation success includes having the product currently in use by target population or in the commercialization stage.

A. Inclusion of firm, university, or clinic partner as determinant of innovation success.

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	.012	.026	.223	1	.637	1.012
	FIRM	.542	.331	2.686	1	.101	1.720
	CLIN	-.415	.323	1.644	1	.200	.661
	UNIV	.086	.372	.053	1	.818	1.089
	Constant	-.470	.329	2.043	1	.153	.625

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	299.064	.018	.024

.

B. Number of alliances with firm, university, or clinic partners as determinant of innovation success.

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	.009	.025	.126	1	.723	1.009
	FIRMA	.089	.062	2.033	1	.154	1.093
	CLINA	-.063	.029	4.765	1	.029	.939
	UNIVA	.047	.036	1.766	1	.184	1.048
	Constant	-.463	.256	3.283	1	.070	.629

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	295.254	.035	.047

Interaction effects between firm age and interfirm alliances

Hypothesis 1 proposed that **young** bioscience firms that engage in firm-firm collaborations are more successful at product/process innovation than young firms that do not. By extension, this hypothesis also makes the argument that interfirm collaborations may not necessarily have a positive association with innovation success for older firms. That is, there is a differential impact of interfirm partnerships for young firms versus for older firms. This interaction effect between firm age and interfirm partnerships was tested using Model 4B.

The data in Table 11 show that the parameter estimates for the **interaction terms, AgeStartUpR*FIRMA and AgeStartUpR*FIRM, were statistically significant** at $\alpha \leq 0.05$. This provided support for the notion that interfirm partnerships have differential effects on young firms (i.e., start-ups) versus older firms with respect to product innovation. The newness of firm moderated the role that interfirm partnerships had on the firm's innovation success. When the model did not include the interaction term (Model 4A), the estimate for the impact of interfirm alliances (FIRMA) was not statistically significant.

A technical interpretation of the values shown in Table 11 is as follows. When the value of AgeStartUp is 0, the interaction term also becomes 0 and drops out, and we are left with the effects of alliances with various types of partners on the reference group (i.e., firms whose AgeStartUp value is 0). When the older firms were the reference group, the coefficient B and Exp(B) values for FIRMA variable were not statistically significant. For these more mature firms, an increase in the number of corporate partners did not have a significant impact SBIR product innovation. On the other hand, when the start-up firms

were the reference group, the parameter estimate for FIRMA was statistically significant and the odds ratio (depicted by Exp(B)) was 1.771. The interpretation of this odds ratio value would be that **for start-up firms, the odds of innovation success increased by over 77% for every additional interfirm alliance** added to the R&D network. That is, **firms having greater number of alliances with other firms were more likely to be successful at innovation.** When the dummy variable, FIRM, was used to test the effect of having a firm partner in the alliance network versus not having any, the odds ratio was 6.530. That is, start-up firms with a corporate partner had greater than 6-fold increase in the odds of successfully innovating than those that did not have a corporate partner. These data provided support for hypothesis 1.

The results from testing Model 4C are presented in Table 11, and they show no interaction effect between firm age and firm-university alliances, which included alliances with universities, federal laboratories, and non-profit research organizations. From this we can conclude that interfirm alliances, but NOT firm-university alliances, have a significant influence in the innovation success by start-ups.

Table 11. Results of logistic regression analysis of interaction between firm age and alliances with university/basic and with firm/corporate partners on innovation success.

Dependent variable is innovation success (INNOV), defined as having the product currently in use by the target population or in the commercialization stage.

A. Baseline model without interaction terms.

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AgeStartUp	.346	.339	1.038	1	.308	1.413
	FIRMA	.093	.062	2.208	1	.137	1.097
	CLINA	-.062	.029	4.674	1	.031	.940
	UNIVA	.049	.036	1.930	1	.165	1.051
	Constant	-.493	.205	5.796	1	.016	.611

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	294.416	.038	.051

B. Interaction between firm age and firm-university alliances (i.e., alliances with university/basic partners).

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AgeStartUp	.138	.421	.108	1	.743	1.148
	FIRMA	.101	.064	2.484	1	.115	1.107
	CLINA	-.063	.029	4.731	1	.030	.939
	UNIVA	.038	.038	.976	1	.323	1.038
	AgeStartUp by UNIVA	.061	.075	.673	1	.412	1.063
	Constant	-.451	.210	4.610	1	.032	.637

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	293.705	.041	.056

Table 11. Results of logistic regression analysis of interaction between firm age and alliances with university/basic and with firm/corporate partners on innovation success (continued).

C. Interaction between firm age and interfirm alliances (i.e., alliances with other firm/corporate partners).

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AgeStartUp	-.173	.420	.169	1	.681	.841
	FIRMA	.074	.063	1.365	1	**.243**	1.077
	CLINA	-.063	.029	4.509	1	.034	.939
	UNIVA	.044	.036	1.487	1	.223	1.045
	AgeStartUp by FIRMA	.498	.254	3.831	1	.050	1.645
	Constant	-.417	.207	4.066	1	.044	.659

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	289.296	.060	.081

AgeStartUp=0 when the firm is older
AgeStartUp=1 when the firm is a start-up

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AgeStartUpR	.173	.420	.169	1	.681	1.189
	FIRMA	.571	.259	4.868	1	**.027**	1.771
	CLINA	-.063	.029	4.509	1	.034	.939
	UNIVA	.044	.036	1.487	1	.223	1.045
	AgeStartUpR by FIRMA	-.498	.254	3.831	1	.050	.608
	Constant	-.590	.376	2.460	1	.117	.554

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	289.296	.060	.081

AgeStartUpR=0 when the firm is a start-up
AgeStartUpR=1 when the firm is older

Table 11. Results of logistic regression analysis of interaction between firm age and alliances with university/basic and with firm/corporate partners on innovation success (continued).

D. Interaction between firm age and interfirm alliance, where the FIRM variable is a dummy variable (i.e., presence or absence of a corporate partner).

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AgeStartUpR	.510	.500	1.039	1	.308	1.666
	FIRM	1.876	.681	7.584	1	.006	6.530
	CLIN	-.384	.329	1.360	1	.244	.681
	UNIV	.058	.376	.024	1	.877	1.060
	AgeStartUpR by FIRM	-1.646	.721	5.206	1	.023	.193
	Constant	-.750	.449	2.788	1	.095	.472

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	293.026	.044	.060

Alliances with *big firms*

In exploring the types of partners that might have a positive effect on the innovation success of small bioscience firms, some additional attributes of corporate partners were analyzed – namely, whether or not these partners were large, well-established companies. The role of "big firm" partners was assessed by testing Models 5A and 5B specified in Chapter 6, and the results shown in Table 12 demonstrated that engaging in R&D collaboration with a large firm greatly and significantly improved the odds of innovation success for small bioscience firms. Specifically, the odds ratio

(Exp(B)) for having an alliance with a big firm partner (BigFirm) was 2.134, indicating that having an alliance with a big firm increased the odds of successfully innovating a product by over 2-fold! Therefore, the data provided support for hypothesis 2, and **firms that had a big corporate partner were more likely to achieve innovation success than firms without a big corporate partner**. Although having a large firm within the R&D alliance network was positively associated with product/process innovation success, increasing the number of large corporate partners in the network did not generate statistically significant further improvement in the odds of innovation success.

Table 12. Results of logistic regression analysis of alliances with big firm partners as determinant of innovation success.

Dependent variable is INNOV, where innovation success includes having the product currently in use by target population or in the commercialization stage.

A. Effect of the presence or absence of at least one alliance with big firm partner

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	.014	.026	.309	1	.578	1.014
	BIGFIRM	.758	.309	6.003	1	**.014**	2.134
	CLIN	-.418	.319	1.722	1	.189	.658
	UNIV	.119	.357	.112	1	.738	1.127
	Constant	-.459	.327	1.968	1	.161	.632

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	295.688	.033	.044

B. Effects of the *number* of alliances with big firm partners

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	.010	.026	.167	1	.683	1.011
	BIGFIRMA	.165	.107	2.407	1	.121	1.180
	CLINA	-.056	.027	4.271	1	.039	.945
	UNIVA	.051	.034	2.243	1	.134	1.053
	Constant	-.470	.256	3.366	1	.067	.625

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	294.690	.037	.050

FDA regulation as an explanatory variable

The descriptive data summarized in Table 4 showed that innovation success rates were much lower for product types that were heavily FDA-regulated. For example, only 5% (3 out of 57) of products in the Research Tools category needed FDA approval for marketing and commercialization, and the rate of innovation success for such products was the highest at 61% (16 in commercialization stage and 19 in use by the target population). On the other hand, 91% of products in the Drugs category (67 out of 74 products) were subject to FDA regulation, and only 8% of those drug products were innovated (6 in commercialization stage and 0 in use by the target population).

In light of these observations and the fact that over half (about 56%) of the SBIR-funded bioscience projects involved developing products subject to FDA regulation (see Table 4), inferential statistics were performed using Model 6A specified in Chapter 6 to determine the impact of FDA regulation on innovation success. The results are shown in Table 13. **The need to obtain FDA approval was a strong predictor of decreased innovation success. As compared to a product that did not require FDA approval, the odds of success in innovating an FDA-regulated product were about 88% lower.** That is, products subject to FDA regulation were more difficult to successfully innovate (i.e., develop and place in the market).

The -2 Log Likelihood statistic measures how well a model can predict; and the smaller this statistic, the better the model. In other words, the log likelihood indicates the model fit, and this value can be used to compare different models to determine which models fit better. The fit of Model 6A was considerably improved when compared to Model 3B, which was the same model without the FDA variable. Adding FDA to the

model reduced the -2 Log Likelihood statistic by 295.254 - 245.914 = 49.34, the χ^2 statistic. In addition to a p-value of .000 for the FDA variable, its Wald chi-square value was greater than 43, which is quite high. While p-value gives statistical significance of the parameter estimate for the FDA variable, Wald gives its importance: higher the Wald, the more "important" the variable. These results indicated the importance of including FDA as a control variable. Therefore, when assessing various explanatory variables or predictors of firm performance, it would be important to control for whether or not the products are FDA-regulated, as this variable alone has great impact. Lumping all bioscience firms together without regard to the non-uniform regulatory pressures could lead to erroneous conclusions about the degree of importance of the explanatory variables under study if the sample being analyzed is comprised of both firms developing FDA-regulated products and firms developing non-FDA-regulated products.

Earlier in this chapter, data derived from using Model 3B indicated that having ties with clinical partners had a negative effect on innovation, which did not make much sense. A possible explanation was that the firms developing FDA-regulated products were ALREADY actively forging R&D collaborations with clinical partners to a greater extent than firms that were not developing such products, so that measuring the impact of clinical partnerships was like measuring the impact of FDA regulation. After controlling for FDA, the negative parameter estimate for CLINA was no longer statistically significant (see Table 13). When hypothesis 1 on the importance of interfirm alliances for start-ups and hypothesis 2 on the importance of having a big firm partner were re-tested after including FDA as a control variable, the prior results and conclusions remained robust (data included in Appendices C and D, respectively).

Analysis of variance (ANOVA) was performed to confirm whether there was a relationship between FDA regulation and the number of clinical partners included in a firm's network of R&D alliances. The results in Table 14 show that, in fact, there was a significant difference between firms whose SBIR supported product is FDA- regulated and firms whose product is not, with respect to the number of clinical R&D partners they had. A one-way ANOVA of the number of clinical alliances according to FDA-regulation status was highly significant with F ratio of 7.349 and $p<.007$. The mean number of clinical partners for SBIR firms developing FDA-regulated products was 4.85 while it was only 2.77 for firms developing non-FDA-regulated products. There was no statistical difference in the between groups variance for the number of university partners and the number of firm/industry partners. **Firms developing FDA-regulated products were already actively forging R&D collaborations with clinical partners and to a greater extent than firms that were not developing such products.**

Table 13. Results of logistic regression analysis of the impact of FDA-regulation on innovation success.

Dependent variable is innovation success (INNOV), defined as having the product currently in use by the target population or in the commercialization stage.

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	.018	.029	.375	1	.540	1.018
	FIRMA	.072	.072	1.001	1	.317	1.075
	CLINA	-.044	.033	1.798	1	**.180**	.957
	UNIVA	.046	.041	1.256	1	.262	1.047
	FDA	-2.077	.315	43.479	1	.000	.125
	Constant	.518	.318	2.654	1	.103	1.679

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	245.914	.228	.305

Table 14. ANOVA to analyze differences in the number of university, corporate, and clinical partners between firms developing non-FDA vs. FDA-regulated products.

		Sum of Squares	df	Mean Square	F	Sig.
UNIV	Between Groups	1.418	1	1.418	.035	.851
	Within Groups	10635.262	264	40.285		
	Total	10636.680	265			
FIRM/ CORPORATE	Between Groups	15.494	1	15.494	1.316	.252
	Within Groups	3109.051	264	11.777		
	Total	3124.545	265			
CLINIC	Between Groups	283.761	1	283.761	**7.349**	**.007**
	Within Groups	10193.581	264	38.612		
	Total	10477.342	265			

		N	Mean Number of Partners	Std. Deviation
UNIV	Non-FDA	119	5.24	6.605
	FDA	147	5.09	6.131
	Total	266	5.15	6.335
FIRM	Non-FDA	119	2.06	3.263
	FDA	147	2.54	3.562
	Total	266	2.33	3.434
CLINIC	Non-FDA	119	2.77	4.604
	FDA	147	4.85	7.259
	Total	266	3.92	6.288

Interaction effects between FDA-regulation and alliances with clinical partners

Hypothesis 3 of this dissertation was that firms collaborating with clinical partners (e.g., hospitals, clinics, medical centers) would be more likely to succeed in the innovation of products subject to FDA regulation than firms lacking clinical partners. Complementarity considerations led to the hypothesis that other firms, particularly big firms, could bring to the alliance the necessary expertise to help these small bioscience businesses overcome major hurdles in product development, such meeting regulatory requirements. Likewise, it was hypothesized that clinical partners might be another external source of complementary expertise to help overcome these hurdles. This was tested with Model 6B containing the CLIN*FDA interaction term (see Chapter 6). Data in Table 15 below show that there was no statistically significant interaction effect of clinical alliances by FDA-regulation on innovation success. FDA-regulated products had a lower likelihood of being successfully commercialized and innovated than those products that did not require FDA approval, but having clinical partners within the R&D alliance network did not improve this outcome.

There are two possible reasons why the data did not support this hypothesis. One is that alliances with clinical partners simply failed to provide access to the necessary complementary assets that could benefit these small bioscience firms. A more likely explanation is that the criteria used to code the clinical partners were inadequate and not rigorous enough. The underlying assumption that collaborators affiliated with clinical departments in medical schools or hospitals had expertise in clinical trials or in the regulatory process was flawed. That is, not all of those collaborating institutions should

have been classified as “clinical” for the purposes of hypothesis testing in this dissertation.

Table 15. Results of logistic regression analysis of interaction between FDA-regulation and alliances with clinical partners on innovation success.

Dependent variable is INNOV, where innovation success includes having the product currently in use by target population or in the commercialization stage.

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	.019	.030	.425	1	.514	1.020
	FIRM	.681	.380	3.202	1	.074	1.975
	CLIN	.145	.473	.094	1	.759	1.157
	UNIV	.182	.423	.186	1	.667	1.200
	FDA	-1.918	.506	14.396	1	.000	.147
	CLIN by FDA	-.485	.660	.541	1	.462	.615
	Constant	.165	.413	.160	1	.689	1.180

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	244.587	.232	.312

Publications and patents

Finally, this dissertation explored how well publications and patents could serve as surrogate measures for innovation success. Publications and patents are frequently used by scholars to represent firm productivity and success, because researchers can easily and independently obtain data on the number of publications and patents generated by firms, without having to survey them. However, whether such measures could appropriately represent project success, in particular innovation success, would depend on whether the predictive values of these output or short-term outcome measures were high. The relationship between the number of publications and patents that result from a project and the ultimate innovation success of the project would need to be strong.

Hypothesis 4 proposed that there is a positive relationship between output productivity, as measured by success in generating publications and obtaining patents, and innovation outcome. In order to investigate whether output measures could predict innovation outcome, data analyses were performed using logistic regression of Model 7A, which contained dichotomous variables PubYN and PatYN for "yes" or "no" on whether any publications or patents were generated from the SBIR project, and Model 7B, which contained integral variables for the number of publications and patents generated (models specified in Chapter 6).

The logistic regression parameter estimates are presented in Table 16 below, and they show that there is no statistically significant relationship between successfully obtaining patents for a product and successfully innovating the product. However, successful publication was associated with successful innovation. A firm that succeeded

in generating publications from the project showed about 3.2 times greater odds of innovation success than a firm that failed to generate any publication from the project.

Table 16. Results of logistic regression analysis of publications and patents as output predictors of outcome.

Dependent variable is INNOV, where innovation success includes having the product currently in use by target population or in the commercialization stage.

A. Effects of the presence or absence of at least one publication or patent output

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	FDA	-2.171	.323	45.199	1	.000	.114
	PatYN	-.207	.329	.395	1	.530	.813
	PubYN	1.167	.391	8.892	1	.003	3.212
	Constant	.117	.347	.113	1	.737	1.124

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	241.020	.245	.328

B. Effects of the *number* of publications and patents generated

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	FDA	-2.164	.320	45.874	1	.000	.115
	Pat	.038	.056	.477	1	.490	1.039
	Pub	.110	.056	3.816	1	.051	1.117
	Constant	.509	.250	4.157	1	.041	1.663

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	242.018	.241	.323

Summary of logit results

Table 17. Summary of logistic regression results of the influence of partner type.

	Effect on Innovation	**Odds Ratio Exp (B)**	**Sig.**	
Firm Age[1]	No effect	1.010	0.683	
Network Size[1]	No effect	1.000	0.992	
FDA Regulation	Negative	0.110-0.130	0.000	88% Decrease in odds of innovation success when product was FDA regulated
Start-Up Firms[2]				
Corporate Partner	Positive	6.647	0.013	Over 6-fold increase in odds of innovation success when a corporate partner was included in network
University Partner	No effect	1.192	0.683	
Clinical Partner	No effect	0.969	0.933	
Older Firms[2]				
Corporate Partner	No effect	1.428	0.383	
University Partner	No effect	1.192	0.683	
Clinical Partner	No effect	0.969	0.933	
All Firms[3]				
Large Corporate Partner	Positive	2.132	0.033	Over 2-fold increase in odds of innovation success when a large corporate partner was included in network

1. Data from Table 9
2. Data from Appendix C; results after controlling for FDA
3. Data from Appendix D; results after controlling for FDA

Based on illustrative case studies, scholars have over the years suggested numerous reasons why establishing alliances with other firms or universities would

increase firm productivity and improve firm performance. However, a review of the literature (presented in Chapter 4) has shown that data from empirical studies are inconsistent in supporting a positive impact of university-firm or firm-firm collaborations on success, as measured primarily in terms of market performance. In addition, prior studies characterizing the types of firms that benefit from alliances have led some scholars to conclude that small firms benefit more, while others have found that larger firms benefit more.

The results of empirical analyses performed in this dissertation have shown that for small U.S. bioscience firms, forming **alliances with other firms was more important for start-ups than for older firms**. For start-up companies, an increase in the number of corporate partners was both positively and significantly correlated with the firms' innovation success, as measured by successful product development to the commercialization stage. Such relationship did not hold for older firms. Moreover, for the start-up firms, forming R&D **alliances with other firms was more important than forming alliances with universities**. An increase in the number of alliances with universities had no statistically significant correlation with an improvement in innovation performance of start-ups nor of older firms.

In addition, the inclusion of a large corporate partner had an effect on innovation success that was not observed in the absence of making this distinction in the partner firm attribute. Analysis of the role of large corporate partners in the network showed that having at least one **alliance with a big corporate partner significantly increased the likelihood of innovation success**, although having additional big firm partners in the network was not associated with further increases in the odds of innovation success.

The number of clinical partners in the alliance network was not positively associated with the likelihood of innovation success. The challenges posed by FDA regulation were a major hurdle to product innovation, and having clinical partners in R&D efforts was not enough to help firms overcome it.

Limitations and Delimitations

This dissertation focused on **R&D** alliances, not downstream market-oriented alliances, such as supplier-buyer partnerships, manufacturing ties, and marketing alliances. It focused on 1) product-specific innovation and 2) innovation success as measured by placement of the product in use by the target population, without regard to how successful the product might be in terms of generating revenues for the firm. In doing so, this dissertation attempted to dissociate R&D success from market/financial/economic success (e.g., profit generation) that might be broadly dependent upon expertise in manufacturing, marketing, sales, distribution, and other post-development processes that are beyond the realm of R&D .

Whether or not firms can innovate successfully is greatly influenced by factors other than R&D competency, such as corporate management and the quality and composition of the management team (e.g., their prior industry experience), the efficiency of business organization and operations, and management of intellectual properties (Ensley & Hmieleski, 2005; Wright et al, 2006). However, these factors were not included in this dissertation research because of difficulties in obtaining data on the extent of the management team's prior experiences with alliances or other qualitative attributes mentioned above. It has been suggested that other challenges encountered in

commercializing disruptive technologies emerging from basic research include identifying the markets in which to apply the technology and estimating the level of demand (Wright et al, 2006). Again, such variables would have been difficult to quantitate and analyze empirically, and were not included in this dissertation research. It would be very hard, for example, to assess and assign a value to one firm's superior market intelligence over that of another.

Furthermore, the drivers of innovation success are many and interrelated in complex ways. In considering **equity financing** that is involved in supporting the development of novel products, for example, it is recognized that one of the most important sources of funding for firms is venture capital financing. This is interrelated with the firm's patent portfolio, which is very important strategically, not only for attracting venture capital but also for defending the market position. Hence, patents have a complex role that is beyond just a reflection of R&D productivity but also function as negotiation capital (Hall & Ziedonis, 2001). Acquisition of public funding, a variable that has frequently been analyzed by scholars of innovation, also has a role in equity financing because public funding can lead to greater chance of acquiring private funding from investors and venture capitalists. Overall, a multitude of influences and factors drive innovation; but to the extent that these can be teased apart and examined only a few at a time, this dissertation has been subject to the same limitations that have affected other empirical studies in this area of study.

Another specific limitation of this dissertation research was that it did not involve measuring the *quality* of partners vis-a-vis their technological or scientific competence, or the quality and nature of interaction between firms and their partners. For example, the

duration of the linkages/alliances was also not measured. Differences in the scope, goals, and management of the partnerships that might affect their effectiveness were not included in the analyses. Although it was possible to identify the collaborators through co-authorship on scientific publications, the nature of the collaborative arrangement or alliance structure (e.g., equity-based joint venture vs. arm's-length contract vs. licensing agreement) could not be determined and was not investigated here. In addition, the complexity of projects could influence their success, but it would have been impossible to objectively measure the differences in the level of complexity of the different projects.

A variable that has been the focus of studies on knowledge spillovers and the formation of regional technology clusters has been the geographic location of firms and universities. For example, studies in the late 80's and early 90's showed that geographic proximity to universities increased innovation by firms, whether innovation was measured by the degree of patenting or the number of new products introduced into the market (Jaffe, 1989). When McKelvey et al. examined whether geographic co-localization was important for formal collaboration in the biotechnology-pharmaceutical sector in Sweden, the results were not always consistent (McKelvey et al, 2003). They examined the firms' regional, national, and international collaborations with other firms and universities, and noted that small firms (<50 employees) that published scientific papers tended to collaborate with university partners located geographically nearby. The authors attributed this observation to easy human capital transfer, in which researchers from universities joined firms or started new firms nearby, while maintaining contact with their colleagues from the university. However, the authors also noticed that university researchers were much more likely to collaborate with international university

researchers than with national firms, which demonstrated that co-location was not necessary for being able to collaborate on scientific projects that resulted in co-authorship (McKelvey et al, 2003). With the exceedingly global nature of biotechnology R&D and today's technologies that have diminished logistic barriers, geographic location of R&D partners was not deemed critical for innovation success and was not analyzed in this dissertation.

Generalizability to non-SBIR companies

Because the data for analysis came from grantees of the NIH SBIR program, there may be some concerns about the generalizability of the results of this dissertation research to non-SBIR companies. Upon considering 1) the eligibility criteria for this program whose funding opportunity is available to the greater biotechnology community without any restriction other than size and 2) the SBIR project characteristics and SBIR firm demographics (e.g., year founded, geographic location) that reflect the patterns observed in the biotechnology community as a whole, it is believed that **the findings are generalizable across the sectors within the greater biotechnology/bioscience industry in the U.S., with one caveat being the size limitation.**

That is, generalizability of the conclusions drawn from this dissertation research would be limited to "small" bioscience firms, since all of the firms that comprised the sample for this study had to meet SBA's size standard of no more than 500 full-time employees. Accordingly, the condition of being small has been integral to the specification of this dissertation's research questions and the hypotheses, and has been

clearly stated throughout this dissertation as one of the defining conditions in the relevant partnering recommendations made for innovation success.

NIH, which is a component of the U.S. Department of Health and Human Services, is the primary federal agency for financially supporting the nation's biomedical research efforts and by far the largest federal agency that funds small firms' R&D effort in biomedicine. Of the federal agencies that participate in the SBIR Program, **NIH is the largest SBIR civilian agency** and the second largest participating agency overall. It spends several hundred million dollars annually (2008 budget of $580 million) to provide SBIR funding to small businesses to assist entrepreneurs in taking their discoveries from the laboratory to market. *These numbers show that the NIH SBIR Program is a significant provider of financing for small firms in the U.S. biotechnology industry*, and it is viewed by this industry as a critical source of seed capital for start-ups and early-stage financing to develop innovative technologies. **Therefore, the impact of the NIH SBIR Program is significant for the U.S. biotechnology industry, as are policy insights generated by analyzing the attributes of SBIR firms and their collaborative R&D activities.**

Aside from the size and ownership criteria, SBIR grants are not restricted to any select group of firms, and there is no bias in funding decisions with regard to whether the firms are rich or poor or whether they are new or well-established. Unlike the Advanced Technology Program administered by the National Institute of Standards and Technology (NIST), for example, which required leveraging of funds from the firms (i.e., companies must provide matching funds to receive government co-support), no such terms are associated with an SBIR grant. So, the firms would not be excluded based on their lack of

financial resources. In the literature, however, the size ranges for classifying firms as either small or medium have been variable. For example, de Jong and Marsili defined small and medium-sized enterprises (SMEs) as firms with no more than 100 employees, making their medium-sized firms much smaller than the U.S. government/SBA-defined small businesses (de Jong & Marsili, 2006).

The SBIR firms can be publicly-traded or privately held. They can be university spin-outs or independent firms. There is no dilution of intellectual property rights or equity. The Program encourages small business awardees to explore their technological potential and provides the incentive to profit from its commercialization. An SBIR grant does not come with obligations that may limit the desirability of this source of government support. **For all of the reasons cited above, there was NO other apparent attribute that could commonly characterize the SBIR grantees as a self-selecting group and there was NO cause for thinking that the findings of this dissertation were subject to *selection bias***. Perhaps the SBIR program would be especially attractive to firms that are not resource-rich and have not yet been able to obtain venture capital or other alternative financing.

Finally, over 75 percent of the SBIR grantees surveyed in 2002 were founded in the period from 1985 through 2001. The SBIR firms were geographically well-distributed across the four U.S. Census Regions. In terms of absolute numbers, more grantee firms were located in the Northeast and West regions, **and this reflects the greater biotechnology industry presence and activity in those areas**.

Uncertainties of R&D

This dissertation research has primarily focused on the impact of collaborations on the successful translation of R&D activities, but there are many other contributing factors, some of which have been mentioned above. In fact, **the greatest unknown and the major source of unpredictability is biology itself**. Because the processes of R&D entail numerous biological/scientific and technological unknowns and uncertainties, it would be nearly impossible to forecast the winners. For that reason, the percentage of R&D projects that are successful in generating a return on investment for firms is notoriously low. Moreover, the evolution and growth trajectory of small firms can vary substantially. Some small firms find a market niche and remain relatively small although still successful, while others pursue radical innovations and eventually become market leaders. As Moore put it, there is no single recipe for success, but rather many profitable niches (Moore, 2003).

CHAPTER 8: DISCUSSION

Policy Implications

About six years ago, NIH launched its Roadmap for Medical Research initiative to much fanfare and declared "bench-to-bedside" translation a priority on the national research agenda. Bench-to-bedside translation refers to taking scientific and technological discoveries generated at the laboratory *bench* within universities, federal laboratories, and other research organizations and turning them into products for application in the clinic to improve the care and treatment of patients at their *bedside*. With collaboration being regarded by policy makers as one of the most effective processes through which translation could be accelerated, there have been numerous initiatives implemented by NIH to promote collaborative R&D. For instance, in 2007 NIH implemented the "multiple PI" policy and, for the first time in its granting history, allowed multiple principle investigators (PIs) to be listed on a traditional research grant (NIH, 2007). Before this policy, a traditional NIH research project grant (i.e., R01 grant) always consisted of a single PI overseeing an independent research project, although the PI could be working with other subordinate researchers and collaborators. In a multiple PI grant, multiple investigators are given equal standing as the PI. Policy makers felt that *multidisciplinary efforts and team science* could be encouraged if more than one PI were recognized on individual awards. All federal research agencies are currently preparing for the implementation of such a policy to formally allow more than one principle investigator on individual research awards (NIH, 2007).

NIH also noted that the difficulties in translating new knowledge to the clinic seemed to be due to a growing barrier between clinical and basic research, and an ever increasing complexity involved in clinical research (NIH, 2008b). For example, with the advent of "omics" technologies such as genomics, proteomics, metabolomics, and glycomics, biomarker discovery research has become highly proficient with thousands of candidate biomarkers being discovered, but only a paltry number of them have made it through the pipeline to clinical use. Specifically, out of over a thousand cancer biomarker candidates discovered by scientists, fewer than ten have been approved by the FDA for cancer screening and monitoring, and the bottleneck in clinical validation and qualification processes has been recognized to be a major obstacle to innovation of point-of-care diagnostic products (Paulovich et al, 2008).

Scholars define *translation* as occurring in two steps: the first step involves transfer of new knowledge and understanding of disease mechanisms gained from basic laboratory research into the development of new methods for diagnosis and treatment, and their testing in humans; the second step involves the translation of the results from clinical studies into everyday clinical practice and medical decision-making (Sung et al, 2003). What translation means to policy makers at NIH is equivalent or comparable to what innovation means to business managers. Translation (i.e., taking basic discoveries to the clinic) is the notion of innovation (i.e., taking new ideas into the market) as conceptualized from a biomedical perspective focusing on a market comprised primarily of patients. This makes research on the factors that affect innovation relevant and informative for policies that affects translation.

The most prominent NIH initiative developed as a solution for advancing our progress in translation has been the Clinical and Translational Science Award (CTSA) program as part of the NIH Roadmap to establish and fund a *national consortium* dedicated to translational research. The consortium is funded through the Institutional Clinical and Translational Science Award (U54) mechanism and managed by the National Center for Research Resources (NCRR), which is a part of the NIH. The strategy behind CTSA is to elevate translational research from a single research enterprise to a *network of collaborations* that bring together diverse perspectives and expertise. The consortium was first launched in 2006 and consisted of 24 medical research institutions located throughout the nation, and in 2008 it was expanded by the addition of 14 U.S. academic health centers in 11 states that are set to receive $533 million in CTSA grants over the next five years to help turn laboratory discoveries into treatments for patients (NIH, 2008a). When the program is fully implemented by 2012, approximately 60 CTSAs are expected to be linked together in the consortium with an annual budget of $500 million.

The CTSA consortium's goals include enhancing the national clinical and translational research capability, training and career development of clinical and translational scientists, and consortium-wide collaborations. The funding and resources provided to the awardees will enable the creation of an academic home for translational research in the form of a center, department or institute that will provide opportunities and resources for original research on novel methods and approaches to translational and clinical science; provide translational technologies and knowledge base for the spectrum of clinical and translational science; integrate translational and

clinical science by fostering collaboration between departments and schools of an institution and between institutions and industry; and provide research education, training and career development of the next generation of clinical and translational (RFA-RM-09-004).

The findings of this dissertation can help facilitate the CTSA consortium aims specifically in the area of public-private partnerships. It is recommended that in initiating partnerships with industry, complementarity considerations should play a role partner selection. While start-ups may be eager to participate in the consortium, the more established firms would be better positioned to help in the translation/innovation process and should be sought out as partners during the initial stages of program growth. This is because a major objective of CTSA is to enhance the translation of discoveries generated at the medical research institutions, rather than to help industry succeed in commercialization per se. The findings of this dissertation on the positive effects of alliances between start-up and other firms are highly applicable when we consider (the laboratories of) the awardee institutions as pre-start-ups. Moreover, the rationale based on complementary assets should lead us to reason that partnerships between universities and old firms might be able to generate greater benefits than the pairing of universities and start-ups, unless those start-ups are spawns of incumbent firms rather than university spin-offs. Once such private-public partnerships are established, CTSA managers should expand the scope of industry partner involvement beyond scientific pursuits and seek their participation in trying to resolve regulatory compliance issues, by working jointly towards improving tasks such as clinical trial registration tracking, IND preparation, and so on.

Whether we are dealing with translation or innovation, the entities that must do the last leg of the work in making technologies and products widely available for the general public are firms rather than universities or hospitals. For this reason, U.S. innovation policies have involved strengthening intellectual property rights, relaxing anti-trust regulations, and providing R&D tax credits **aimed at incentivizing businesses**. By providing additional insights into what is required for small businesses to innovate successfully, the findings of this dissertation research can inform the expansion of existing programs and the design of new initiatives by federal agencies that support biomedical R&D. Once public-private partnership building under CTSA has demonstrated some progress, this program could be expanded to later include young firms and start-ups, and facilitate their relationships not only with the research centers that are consortium members but also with the incumbent firms that have already been participating in the consortium.

Practitioners (i.e., business managers) strategically seek out opportunities to form alliances with other firms during all stages of firm development, but this dissertation research has demonstrated that engaging in interfirm alliances was particularly important for start-ups in order for them to have greater likelihood of innovation success. These young firms are often caught in a catch-22 situation because it is nearly impossible for them to get potential corporate partners to be interested in them during the early start-up stage when they lack social and commercial capital and their track record is nonexistent. For most start-ups with therapeutic or diagnostic products not yet at the clinical development stage, their options for partnerships tend to be limited to academic or federal researchers. A program that is centered on assisting start-up companies would also be

well-aligned with the economic development mission of state governments and should be considered by organizations such as the Technology Development Corporation (TEDCO) in Maryland and its counterpart in other states. TEDCO was created by the Maryland State legislature in 1998 "to be Maryland's leading source of funding for technology transfer and development programs and entrepreneurial business assistance" (http://www.marylandtedco.org/abouttedco/whoistedco.cfm).

Another finding of this dissertation was that alliances with big firms had a positive effect on innovation. A policy solution to incentivize the well-established big firms to partner with small companies could involve federal subsidization of the risks involved in product development. An example of this type of program is the National Institute of Standards and Technology's Advanced Technology Program (ATP), which was replaced by the new Technology Innovation Program (TIP) in 2007 when the President signed the America COMPETES Act (H.R. 2272). The goal of ATP was to "bridge the gap between the research lab and the market place" (ATP, 2005). In ATP, the government shared in the high development risks; and in doing so, the program imposed strict cost-sharing conditions that promoted collaborations. According to ATP policies, large Fortune-500 companies participating as a single firm had to pay at least 60 percent of the total project costs, but two or more companies working together had to pay at least 50 percent of the project costs (ATP, 2005). In addition**,** single company projects were funded for no more than $2 million total over a maximum period of three years, but for joint venture projects there was no limit to the size of the award to be funded over a maximum period of five years. Such funding structures provided an incentive for firms to form joint ventures rather than apply as a single company.

When scholars examined some failed high technology strategic alliances to find out why such efforts failed, they determined that the causes were unpredictable, external forces beyond the control of the firms, such as tax policies and regulatory environments (Bruton & Samiee, 1998). Bruton and Samiee focused on one high technology strategic alliance in particular: an international alliance that was established in 1993 between International Business Machines (IBM) Corporation and Kvant in Russia. Kvant was established by the Soviet Union in 1984 to manufacture personal computers for military use and became privatized after the 1991 revolution. IBM's goal in forming the alliance was to gain market entry in Russia. Kvant's motivation in pursuing the alliance was to gain know-how in Western manufacturing, quality control, and management methods. IBM provided the parts, and Kvant used the equipment supplied by IBM to assemble the computers. The authors noted that the formation of IBM-Kvant alliance appeared to have been done in a "textbook-like manner," in which the processes of selecting a partner, negotiating the alliance, and setting the partnership in motion followed good business practices. In 1996, however, IBM withdrew from the alliance, which was deemed as "failure" because the opportunity costs associated with this alliance were quite large (Bruton & Samiee, 1998). It turned out that the overwhelming motivation for IBM in forming the alliance was the potential cost savings resulting from tariff-free import of components. Six months after the alliance began, however, the Russian government unilaterally reversed its commitment to tariff-free parts importation.

Although not a high technology strategic alliance, Proctor and Gamble's (P&G) alliance with a chemical plant in Chevchenko, Kazakhstan was also examined (Bruton & Samiee, 1998). P&G's strategy was to transfer technical and manufacturing know-how to

its Russian partner, enabling it to produce P&G's toothpastes for the Newly Independent States markets. This venture failed primarily because Kazakhstan's poor tax policies and other regulatory problems made it difficult to operate the venture profitably (Bruton & Samiee, 1998). In trying to identify factors within the alliance that could account for the failure, the authors noted that it was the partners' inability to correctly predict forces in the Russian market. They pointed out that a lesson learned from these case studies was to choose an "internationally competent" host-market partner who would be personally well-networked with the bureaucratic structure of government offices and could obtain timely procedural and regulatory information that might otherwise be unavailable (Bruton & Samiee, 1998). What the authors failed to point out but has policy pertinence is that financial incentives were critical in the decision-making by large firms to form as well as dismantle the alliances.

Therefore, it would be possible to promote the participation of big firms in interfirm collaborations by providing financial incentives established through public funding or cost-sharing by the government when a large firm undertakes an R&D project jointly with a small firm partner. Similarly, initiatives with the objective of assisting start-ups attract corporate partners could be crafted with language in the eligibility criteria that require the lead partner in a joint venture that applies for government funding to be a start-up firm. This could promote their desirability as partners to other firms. While it may not be feasible to establish this type of program in an agency such as the NIH whose principal constituency is the academic community, our Congressional policy makers could provide for the creation of industry-oriented programs in other agencies through appropriations. For example, members of the Senate Committee on Small Business and

Entrepreneurship or the House Small Business Committee could encourage the Small Business Administration to consider such programs.

Other than acquisition contracts, the SBIR program is the primary way that the NIH supports industry. While non-regulatory agencies such as the NIH can't control internal firm management practices or dictate how an industry should operate, they can establish policies that have a stimulatory role and encourage desired responses and actions from the grantee firms. Informed by the finding that bringing together certain types of partners for collaborative R&D can increase success in innovation, agency policies could incorporate conditions for public funding that incentivize such interactions.

In May of 2008, the National Cancer Institute (NCI) announced that it would devote $10 million annually toward a new initiative known as the Bridge Awards program to complement the SBIR program. The program was developed as a possible solution to the fact that many small bioscience and biotechnology companies have great difficulty overcoming a funding hurdle to advance their drugs from the pipeline into clinical trials. The program's objective is to help small businesses cross this "valley of death" – i.e., capital gap between the *research/early development* phase and the *later development/commercialization* phase in product innovation (Nair, 2008). Bridge Awards with a budget of up to $1 million per year for a period of up to three years would be provided to help sustain companies from the second to the third SBIR phase. Currently, the initiative has been crafted to give an advantage in competing for this award to companies that successfully secure matching funds from other sources, but the findings of this dissertation would suggest that special considerations (e.g., more favorable review

score) should also be given to companies that succeed in securing a large corporate partner for product development.

A principal rationale for the government's support of R&D programs has been to remedy market failure, stemming from the fact that a firm is not going to invest in R&D if a significant portion of the social benefits from the new knowledge, technology, and product generated by the R&D cannot be captured by the firm. According to Jaffe, programs such as the ATP should therefore seek to maximize the social rate of return from the expenditures they make, and he has suggested that ATP's project selection should be based on which of those will generate large spillovers (i.e., social benefits that are not captured by the firm conducting the R&D) (Jaffe, 1998). Jaffe has also noted that social returns and spillover benefits cannot be realized without successful commercialization of the new technology because market spillovers depend entirely on commercialization and knowledge spillovers are largely dependent on commercialization (Jaffe, 1998). When innovative technologies and product ideas just sit on the shelf, they do not benefit the customers and are unlikely to create much spillover effect, knowledge spillover being limited and market spillover nonexistent. Expected returns are a function of the magnitude of the return times the probability of success (Jaffe, 1998). If public policy is to maximize social returns, then an obvious policy relevance of the findings of this dissertation on R&D alliances is that the information can be used to increase the probability of success and thereby increase social returns to R&D. Unless novel discoveries and technologies are successfully brought to market, there are no innovations to speak of and what we are left with are just great ideas.

Another policy relevance of the findings of this dissertation is that they could somewhat help overcome the FDA regulatory burdens on innovation. According to the Pharmaceutical Research & Manufacturers of America (PhRMA), scientific and regulatory barriers to innovation and the costs of innovation have climbed over the years, requiring 10-15 years of R&D effort and $1.1 billion in investment for product innovation (Loew, 2004). The regulatory burden that is attributed as one of the factors driving the decline in performance is partly due to the increasing FDA variability across its Divisions and the uncertainly around FDA expectations and requirements (Loew, 2004). The mantra among other bioscience groups is similar: "Regulatory burdens, rising costs hinder innovation in drug and device industries" (Hasson, 2009). According to a 2008 member survey conducted by the Advanced Medical Technology Association (AdvaMed), the factor that most negatively affected innovation in medical technologies in recent years was FDA regulatory requirements (84%); other leading factors were cost of clinical research (74.1%), Medicare coverage and reimbursement requirements (71.6%), research and development costs related to movement into new markets (66.7%), and U.S. private payer coverage and reimbursement requirements (63.9%) (Hasson, 2009).

On average only 8% of products currently in phase I clinical trials will ultimately receive FDA approval, while the average non-capitalized cost of pre-market trials is $403 million per medication and $100 million per device (Hasson, 2009). Even with definitive preclinical data and promising early trial results, many pharmaceutical compounds actually fail in demonstrating adequate evidence of safety and efficacy during the final stage, full-scale, confirmatory phase III trials conducted before marketing approval

(Christensen et al, 2007). This is the risky and uncertain nature of the drug discovery process. The costs of clinical trials and regulatory requirements go hand in hand since it was the FDA that determined that large, randomized, controlled clinical trials were the 'gold standard' for pre-marketing efficacy data generation (Christensen et al, 2007). A detailed discussion of clinical trials and other FDA requirements has been presented in Chapter 2.

As expected, the data from SBIR grantees demonstrated that innovation success rate was much lower for product types that were FDA-regulated. For example, over 90% of products in the Drugs category were subject to FDA regulation, and only 8% of them were innovated. Only 5% of products in the Research Tools category needed FDA approval, and innovation success rate for such products was the highest at greater than 60%. The majority of innovation successes achieved was for product types that did not require FDA approval, such as tools and software. Inferential statistical analysis showed that the requirement for FDA approval was a **strong predictor** of **decreased** likelihood of **innovation success,** where the odds of success in innovating an FDA-regulated product were about 88% lower than for a product that did not require FDA approval.

FDA's mission is to promote public health by supporting the development of safe and effective treatments, and lowering the standards for pre-market data submission would not be an option. Some sources have recommended increasing the academic-industry interactions to help overcome the challenges of regulatory hurdles (Hasson, 2009). The position of this dissertation is that interfirm alliances between entrepreneurial start-ups or university spin-offs and large pharma or large biotech could help spur clinically beneficial innovations. While FDA regulation decreased the likelihood of

innovation success, interfirm alliances between start-ups and established firms or between small firms and big firms helped increase the likelihood of innovation success, after **controlling for the effect of FDA regulation**. This can also be viewed as helping to overcome the costs of FDA regulation, since these are sunk costs (development costs) that could provide a return if innovation is successful.

Moreover, these alliances could help overcome the costs of FDA regulation by enabling firms to learn ways to become more efficient in R&D. This dissertation's main rationale for hypothesizing the benefits of particular interfirm alliances was that they provided access to complementary assets, such as tacit knowledge regarding regulatory compliance. Such knowledge could involve better design of randomized trials with wise choice of comparison groups, for example. This theorizing is supported by a recent publication in which the author has found that medical device start-ups founded by former employees of incumbent firms perform better than other new entrants, and states that this superior performance in innovation is not driven by technological spillovers from parent to spawn, but rather by non-technical knowledge related to regulatory strategy and marketing (Chatterji, 2009).

A programmatically important observation from analyzing the SBIR data was that diagnostics constituted a very small fraction (less than 10%) of products whose R&D was supported through NIH SBIR funding. It is not clear whether this was due to the fact that only a small number of diagnostics-related applications were submitted or because only a small number of them received fundable scores. Regardless, it would be worthwhile for the NIH to explore new ways to promote applications from the diagnostics industry. The SBIR data have shown that diagnostics firms were by far the least likely to engage in any

kind of R&D collaboration. Almost 50% of them had no linkages with other firms or with clinical partners. For those diagnostics firms that did engage in interfirm R&D alliances, CROs and service providers comprised the greatest proportion of the partner firms. A possible explanation for this observation is that the core competencies of pathology service laboratories and laboratory testing service providers, which were classified under CRO, had the greatest complementarity to the immediate needs of diagnostic firms. In light of the dismal rate of product innovation by diagnostics firms and our paucity of SBIR support that is directed at this group of firms, additional programs that complement the SBIR program might be worth developing. Also, the aforementioned policy strategies aimed at promoting the inclusion of small and young firms in interfirm collaborations could be extended to promote the inclusion of diagnostics firms.

Fostering the R&D efforts of diagnostics companies would be particularly relevant in light of the medical community's growing interest in personalized medicine, for which biomarkers have a critical role to play. Biomarkers are molecular, biological, or physical attributes that can be objectively measured and that can characterize a specific underlying physiological state to help detect, identify, and classify disease into subtypes (diagnostic biomarkers); stratify risk of disease progression in patients (prognostic biomarkers); or predict or quantify responses to specific therapy (predictive biomarkers) (Wilson et al, 2007). Such biomarkers would enable us to establish tailored therapies and monitor responses to treatment, and they are emerging as key indices for "personalized" or "individualized" patient management. Because biomarkers can provide direction and influence critical clinical decision-making regarding expensive or complex therapeutic

interventions, they can indirectly but substantially influence healthcare economics and the allocation of healthcare dollars.

We are thus beginning to see considerable activity in biomarker R&D, but the success rate in biomarker innovation has been dismal. Despite our ability to generate thousands of candidate protein biomarkers, diminishing numbers (only 0 to 2 per year in the recent years) have been achieving FDA approval (Anderson & Anderson, 2002; Paulovich et al, 2008). A number of biomarker researchers have noted that one of the major problems may be that most of these biomarker candidates do not have defined disease management value in the form of clinical qualification, and relationships describing the clinical utility of biomarkers need to be assessed prospectively in blinded and randomized clinical trials, and subsequently validated in follow-up trials (Dalton & Friend, 2006; Wilson et al, 2007; Wilson, 2006). In other words, these biomarkers are not being successfully innovated because they are short of being adequately developed clinically. Moreover, although the technologies that produced these biomarkers have been prolific as discovery engines, they have not been systematically translated into assays with robust performance compatible with clinical laboratory practice (Wilson et al, 2007).

Like the drug discovery pipeline of the pharmaceutical industry, the biomarker pipeline of the diagnostics industry has been experiencing a high failure rate. But the diagnostics industry as a whole is at a greater disadvantage because diagnostics have historically been perceived as being of lesser value than drugs and they have been reimbursed at significantly lower levels than therapeutics. Other scholars have noted that this inadequate reimbursement has been a major economic impediment to the

development of new diagnostics (Phillips et al, 2006). As alluded to earlier, the emergence of molecularly targeted therapies are generating interest among big pharma to bring new predictive biomarkers/tests into clinical use to help identify those patient who will respond to their drugs versus those who will not. Development of therapeutics and predictive biomarkers concurrently through a joint R&D effort of collaborating pharmaceutical and diagnostics firms could result in greater innovation rate.

It has been shown in prior work that the chemicals industry, for example, has the largest share of firms collaborating with universities while telecommunications service firms are the least involved with universities (Fontana et al, 2006). A finding of this dissertation from analyzing the distribution of the types of partners that comprised the network was that dedicated biotechnology and pharmaceutical firms had similar tendencies with respect to the linkages they formed with different types of partners. Both biotechnology and pharmaceutical firms tended to collaborate with basic/academic research institutions (i.e., universities, federal laboratories, and non-profit research institutes) over the other types of partners, with greater than 75% of biotechnology and pharmaceutical firms having one or more linkages with academic/basic research institutions. When they formed alliances with other firms, the biotechnology firms tended to form alliances with other biotechnology firms while the pharmaceutical firms tended to form alliances with other pharmaceutical firms. Although these small biotechnology firms could have benefited greatly from networking with and gaining know-how from the pharmaceutical firms, the reality was that similar firms tended to network with each other. These findings reinforce the argument that policy interventions might be necessary

to stimulate the types of partnering that could positively affect innovation because such partners are not likely to come together on their own.

What would be interesting for future research is to examine the complementary fit among partners in an alliance network, not in terms of whether they are corporate, academic, or clinic as has been done in this dissertation, but rather in terms of different biomedical disciplines/areas of specialty or the different bioscience subsectors that could be brought together for synergistic benefits. In 2009, NCI has set aside over $100 million over a five year period for a collaborative network of Physical Science-Oncology Centers (PS-OC) that will bring together experts from the physical sciences / engineering and cancer biology / oncology fields (RFA-CA-09-009). Research examining the complementary fit of different disciplines could provide additional insights into the potential impact of these other types of partnering combinations, and have policy implications for programs such as the PS-OC.

In the current challenging economic environment of flat budgets, federal agencies such as the NIH must grapple with difficult choices concerning its myriad programs. The NIH must consider where the greatest scientific and innovation opportunities lie, which programs to invest in at the present, and which programs to scale back or eliminate. The findings from this dissertation and other similar studies on alliances could inform and assist in the decision-making not only of which collaborative programs to support but also which entities should be the target of these programs to produce the greatest public health benefit and highest return on the public investment in biomedical R&D.

Insights for Managers

This dissertation's investigation into R&D partnering that could help firms achieve innovation has been practically motivated by the recognition that forming alliances is a fundamental practice within the biotechnology industry. Partnering is no longer just a part of the competitive strategy of firms, but it has come to be predominantly viewed as a "business imperative" by firm managers in this industry. This is quite evident, for instance, when we examine the Biotechnology Industry Organization's conference proceedings, program agendas, and keynote speaker selections over the past few years that have always included a focus on some aspect of alliances and partnerships (http://bio.org/events/past_events.asp ; http://midatlanticbio.org/conference/keynote-speakers/).

The importance of having the right alliances during the start-up stage has been stressed by scholars such as Baum et al., who go so far as to assert that firms that fail to configure effective alliance network at the time they are founded will be inferior competitors at *every* age (Baum et al, 2000). According to the findings of this dissertation, it would be particularly important for start-ups to establish alliances with other firms. However, the beneficial impact of interfirm alliances was moderated by firm age, whereby having interfirm alliances was not as important for innovation by the older firms. The notion that alliance networks evolve, as partnerships formed during a firm's formative years get replaced by others as the firm matures and requires different sets of expertise, makes theoretical sense when we draw upon the notion of complementary assets discussed throughout this dissertation. That is, network composition should be dynamic to be competence-building through the different stages of firm's growth.

This dissertation also showed that network size did not have any positive effect on a firm's innovation success, thus providing partial support for Baum's claim that increasing the number of alliances without attention to partner diversity could result in inefficient networks (Baum et al, 2000). However, the findings of this dissertation did not reflect Goerzen observation that a propensity for repeat partnerships had a negative influence on corporate performance (Goerzen, 2007). Small bioscience companies do not have many partnering opportunities with other firms, and they frequently do engage in repeated alliances with partners from previous R&D projects. This dissertation dealt with the total count of all alliances (including redundant ties) in the analyses but preliminary data (not shown) using the total count of unique partners (non-redundant ties) had not led to different results or conclusions. A firm that collaborated multiple times with only one or two unique partners was as likely to succeed as a firm that partnered only once with multiple partners.

All of these results highlight some important considerations for start-up bioscience firms in their management of alliance portfolios and judicious partner selection. Some prescriptions for these very young firms would include paying attention not only to the obvious issues involving research and scientific fit but also the partner type. Multiple alliances with just academic partners, while easier to cultivate might result in fewer innovations than building a network of alliances with a mix of academic and corporate partners.

The resource-based view of the firm informs us that firms can achieve sustainable competitive advantage by possessing rare and hard-to-imitate resources, but this theory has little operational validity because advising practitioners to simply acquire such

resources is not practicable (Priem & Butler, 2001). Operational validity, as defined by Thomas and Tymon, is the ability of practitioner to implement the action implications of a theory by manipulating its causal (or independent) variables (Thomas & Tymon, 1982). The insights generated by this dissertation research are practicable in that forming new partnerships and discontinuing old ones at a given time is within the strategic control of firm managers; and through these activities, hard-to-imitate resources and competencies could be gained. By making specific actionable recommendations, this dissertation helps confer operational validity, albeit indirectly, to the resource-based views of the firm.

Importance of Context in the Study of Alliances

Understanding the dynamic workings of a particular industry (e.g., the learning process, organization, and behavior of the firms in their function of developing and producing goods and services) and taking into consideration the proper context for that industry as part of the analysis is critical for accurately interpreting any research findings and realizing their limitations. Foremost should be the recognition that institutions and organizations that comprise a firm's external environment shape the behavior and actions of firms, and influence their strategic partnerships and network formation with other firms and organizations. Hagedoorn and Duysters have suggested that various technological environments, for example, should be examined to ascertain the *differential* effects of network characteristics on performance (Hagedoorn & Duysters, 2002). **These considerations provide a number of reasons why the findings of this dissertation, which have been based on data derived from three bioscience subsectors – biotechnology, pharmaceutical, and diagnostics – in the United States, might not be**

generalizable to similarly young or small firms in other sectors or to the same sectors in other countries. These three subsectors are founded on a common scientific knowledge base that is biological/biomedical in nature, are characterized by research-intensive organizational activities, and are subject to similar environmental/external (e.g., market, regulatory) context. It would be hard to declare with certainty that existing differences in some of the major variables embodying the structure and operations of a sector, as elaborated in greater detail in the following subsections, will not differentially affect the network learning implicit in the types of partnering recommended in this dissertation.

Regulatory environment

One context that has been examined in this dissertation was the regulatory environment. The results from this dissertation showed that by far the single MOST IMPORTANT factor that determined the likelihood of innovation success was whether or not the product needed to have approval by the FDA. The significance of this observation is that it highlights an important but overlooked difference of the biotechnology and bioscience sector from most other sectors that have been the subject of prior alliance research. **The types and structures of relationships, including R&D partnerships, that affect innovation success by firms in those other industries may not be generalizable to the firms in the biotechnology industry (and vice versa) because of the unique regulatory environment in which the biotech firms must operate.** In the absence of accounting for moderating factors, such as FDA regulation, one could overstate the significance of the impact of certain types of alliances. As Mowry has

noted, the types of policies and organizational structures that support effective R&D can differ considerably not only among different industries, but even for different academic disciplines and research areas (Mowery, 1998). It would be erroneous to think that the findings and policy implications based on the analysis of data from diverse industries and sectors, such as manufacturing and software, could be applied to the bioscience sectors just because they all share a certain attribute, such as being "technology-driven." FDA regulations are binding on the activities of the pharmaceutical/biopharmaceutical sector, but for the software sector, it is standards-setting that is binding.

Sectoral differences

There are major differences across sectors that preclude the generalizability of the results from this dissertation to other sectors or to the same sectors in other countries, and some key diversities highlighted by Malerba help support this assertion. First, the knowledge base that is a key element in a sectoral system may "**greatly differ across sectors** and affects the innovative activities, organization and behavior of firms within a sector" (Malerba, 1999). Agents involved in the knowledge flow differ for different sectors, which means that effective partnerships may need to take on different membership characteristics for different sectors. In the pharmaceutical sector, critical knowledge about the product (e.g., the clinical efficacy of drugs) must be acquired from the patient population enrolled in clinical trials as part of the R&D process before the product can get marketed. In the software sector, knowledge regarding software applications is obtained from the users as part of response to market demand.

Secondly, Malerba points out that the role of "**non-firm organizations and institutions greatly differ across sectors** and affect the innovative, and productive activities of firms" (Malerba, 1999). For instance, the organizations that played a significant role in the growth of the biotechnology sector were universities, but for the semiconductor and computers sector, the organization that had a similar effect was the military. The *evolutionary theory* of economic change, which places emphasis on beliefs and expectations that are affected by previous learning and experience, as well as the environment in which the agents operate (Nelson, 1995), also presents similar consideration of institutional differences that cast uncertainty over the generalizability of the findings of this dissertation to other sectors. For example, in the information technology (IT) sector, the suppliers of components and subsystems (e.g., microelectronics suppliers) play a major role in affecting the competitiveness of downstream IT producers (Malerba, 1999). Such is not the case for in biotechnology sector. In the machine tools sector, innovation is incremental, R&D is not done extensively and R&D cooperation is not common in small firms, but vertical producer-user links as well as partnerships with customers are common and play a major role (Malerba, 2005). *For such a sector whose small firms do not conduct R&D, recommendations of this dissertation pertaining to R&D alliances would not be applicable or relevant.* In the software sector, the spread of network computing, the internet, and the development of open system architectures and open source have led to the decline of large computer producers as developers of integrated hardware and software systems (Malerba, 2005). *For such a sector, the recommendation of this dissertation for interfirm alliances with large firms may not be useful or appropriate.* As

Malerba puts it, the learning patterns, behavior traits, and organizational forms of agents are *constrained and bounded* by the knowledge base and the institutional context in which the firms act (Malerba, 2005).

The interactions among agents are shaped by institutions that are specific for different sectors, such that the resulting network characteristics would be specific to those sectors. For example, in the case of biotechnology and pharmaceutical sector, networks are formed among large pharmaceutical companies, new biotechnology firms, and universities; while in the machine tools sector, the networks are composed of producers, users/user firms and local banks (Malerba, 1999)). In the software sector, the internet is the means for collaborative innovation, and the distribution of software products (Malerba, 2005). National institutions such as intellectual property rights can also have differential effects on different sectors. Policies that may be good for some sectors, even if they are technology-based, may not be good for biotechnology, as demonstrated by the fact that the Patent Reform Act of 2007 (H.R. 1908, S. 1145) was lobbied for vigorously by the software and IT industries but was adamantly opposed by BIO (Biotechnology Industry Organization). While intellectual property rights are important for ensuring appropriability and patents are critical assets used in determining the value of a firm's technology in the biotechnology sector, such is not the case in the computer software sector with its open source movement. Institutions undoubtedly play a major role in affecting technological innovation and the organization of activities surrounding innovation across all sectors.

Cross county differences in national innovation systems

National innovation systems can be quite different not only from one sector to another, but also from one country to another. While the same sector in different countries would not differ in dimensions pertaining to products and basic technologies because according to the standard economics definition of sectoral boundaries, they should have similar production processes (technological similarity) and functions of the products (functional similarity), the sectors in different countries would face different strategic and organizational choices subject to institutional conditions. According to Malerba, networks for the machine tools sector differ from country to country because different users and demand structures have led to different innovation systems, whereby local financial institutions, internal and regional labor markets, and trust-based relationships at the regional level play a major role in influencing competitive advantages in specific areas (Malerba, 2005). *While Malerba argues that the patterns of innovative activities for a specific sector are similar across countries, he also states that "this is so as long as opportunities, appropriability and cumulativeness conditions are rather similar across countries"* (Malerba, 1999). The ability to generate and exploit opportunity conditions may not be similar across countries because this ability is related to the presence and effectiveness of science-industry bridging mechanisms, vertical (supplier-user-producer) interactions, and horizontal links among firms in the organization of innovation activities. When the pharmaceutical sector was confronted with changes in the knowledge base, transformations in the behavior and structure of the agents and in their relationships with each other resulted, but the specific ways in which these transformations occurred across countries have been profoundly different due to the

details of the institutional structure of each country (Malerba, 2005).

In conclusion, the above examples from the software, machine tools, and biotechnology sectors highlight some specific differences across sectors in firm behavior and strategies, and networking. National institutions such as intellectual property rights and anti-trust regulations have different effects on innovation by different sectors. They also show that certain institutions that are important for one sector may not have much relevance for another sector. Moreover, counterpart institutions in different countries may take on different features and affect innovation differently. These differences could, therefore, limit the generalizability of the findings of this dissertation that focused on firms whose operations were subject to U.S. institutions and U.S. socio-economic context. The results would be generalizable to the extent that the sectoral and national innovation systems are comparable (e.g., the agents through which the path of knowledge flow and accumulation are comparable, the distribution and diffusion of competencies are comparable, and the types and nature of vertical and horizontal relationships among the various agents are comparable). Otherwise, policies that integrate the recommendations of this dissertation may have a different impact on non-bioscience sectors. Perhaps insufficient understanding of context and the absence of appropriate control variable could explain the conflicting findings reported by different researchers regarding the benefits of various alliances, as reviewed in Chapter 4.

Relationship Between Short-Term Outputs and Long-Term Outcomes

Finally, although not a major research question addressed in this dissertation, the relationship between short-term R&D outputs and long-term outcomes, and whether

output measures (i.e., publications and patents) could predict innovation outcomes were also examined. This analysis helped assess the validity of employing output measures as substitutes or surrogates for measures of success when such outcome measures are difficult to obtain. In the literature, these output measures have been used frequently as indicators of firm productivity from which conclusions about firm performance were drawn. The results of this dissertation study showed that firms that succeeded in generating publications from the project were more likely to succeed in innovation than firms that failed to generate any publication from the project. These findings help corroborate the practice of assessing a firm's performance level based on its publication record.

GLOSSARY

Appropriability: The conditions surrounding an invention that enable the capture (or claiming rights to) the value of an innovation (i.e., reap profits generated by an innovation). Appropriability is necessary to make more money than the cost of R&D. Strategies to ensure appropriability include patents, branding, gaining lead time and exploiting a learning curve.

Average linkage: The average of all possible permutation of distance measures between individual points in one cluster and individual points in the other cluster.

Biotechnology: Technological application that uses biological systems or biological derivatives to make or modify products or processes.

Centroid: Distance between the center of mass of points in one cluster to the center of mass of points in the other cluster.

CESPRO: Center for Research on Internationalisation (CESPRO) at Bocconi University, Milan, Italy

Competence building: Process by which a firm achieves *qualitative* changes in its existing stock of assets, resources, and capabilities (i.e., creates *new* strategic opportunities to develop products that are new sources of cash flows).

Competence leveraging: Process by which a firm sustains its existing assets, resources, and capabilities and deploys them in ways that do not require qualitative changes in them.

Complete linkage: Distance between a point from one cluster and a point from another cluster that are the farthest apart from each other and that represents the maximum distance between the two clusters.

Contract research organization (CRO): A person (i.e., a legal person, which may be a corporation) that assumes, as an independent contractor with the sponsor, one or more of the obligations of a sponsor, e.g., design of a protocol, selection or monitoring of investigations, evaluation of reports, and preparation of materials to be submitted to the Food and Drug Administration. [21 CFR 312.3(b)]

Cross-validation: Remove a point from dataset, rebuild the classifier, and determine how well the point that was left out does on the new classifier.

Dynamic capabilities: Firm's ability to integrate, build, and reconfigure internal and external competences to address *rapidly changing environments*.

Epistemology: Epistemology or "theory of knowledge" is the branch of philosophy that studies the nature and scope of knowledge. It also deals with the means of production of knowledge. Epistemology primarily addresses the following questions: what is knowledge, how is knowledge acquired, and what do people know.

Innovation: A new idea, practice, or object that is successfully brought to market. There are four types of technological innovation: incremental, generational, radical, and architectural.

Institutions: Norms, routines, common habits, established practices, rules, laws (e.g., patent laws), and standards, which may range from the formal (e.g., laws and regulations) to informal (traditions, conventions), and systems such as the financial system, education, and labor markets.

Invention: Breakthrough discovery.

Joint R&D agreement: Involves the pooling of resources by two or more partners for the purpose of sharing technology, know-how, and setting up a joint R&D program.

Logistic regression: Applies maximum likelihood estimation after transforming the dependent into a logit variable (the natural log of the odds of the dependent occurring or not). In this way, logistic regression estimates the odds of a certain event occurring.

Market failure: A situation in which the market fails to efficiently allocate resources for the greatest public good.

MERIT: Maastricht Economic Research Institute on Innovation and Technology (the

Netherlands)

Network efficiency: Defined as diversity of capabilities per alliance and measured by Hirschman-Herfindahl index: one minus the sum of the squared proportions of the firm's alliances with each of the partner types, divided by the firm's total number of alliances (Baum et al, 2000). For example, a firm with six alliances – five with pharmaceutical firms and one with a clinic -- would score .046 for its network efficiency. $[1-(5/6)^2 + (1/6)^2]/6=.046$

New independent firms: Firms founded by non-university affiliated entrepreneurs.

Odds: Odds of an event (e.g., innovation success) happening is defined as the probability that the event occurs divided by the probability that the event does not occur. This is estimated by the ratio of the number of times that the event occurs to the number of times that it does not. When odds equal one, the probability of the event happening is equal to the probability of the event not happening. In other words, when the odds ratio is 1, there is no relationship.

Odds ratio: The ratio of the odds of an event (e.g., innovation success) in one group (i.e., exposed group) to the odds of the same event in the other group (i.e., not exposed group).

Organizational structure: The allocation of use rights of firm's assets, decision rights over firm's assets, and income rights of employees (e.g., stock options, profit sharing

schemes) (Stieglitz & Heine, 2007).

Pharmacogenomics: The biomedical discipline that relates changes in gene structure on drug effects. Classical pharmaco*genetics* involved identifying a genetic basis for pharmacologic response. Modern pharmaco*genomics* looks at the variability in the genome first, and then attempts to find an associated drug effect.

Probability: The number of times the event (e.g., innovation success) occurs divided by the number of times the event could occur.

Research contract: One firm, typically a larger firm, contracts another, usually a smaller firm, to conduct research in the development of a specific technology.

Research joint venture: Two or more separately owned companies formally agree (i.e., sign a Joint Venture Agreement) to collaborate on R&D within a distinct organizational entity or "company" that is characterized by common equity ownership. All involved contribute to the cost-sharing requirement. Such equity-based joint ventures typically serve the purpose of substantially lowering the transaction costs between the independent research partners (de Jong & Marsili, 2006).

Schumpeterian patterns of innovation: Patterns of innovation are classified into two alternative groups. A "widening" or "creative destruction" pattern of innovation in industry is characterized by technological ease of entry and innovation generated mainly

by the entrepreneurial activity and creativity of small, newly founded firms. The innovation base widens as entrepreneurs enter the industry with new ideas and products, launch new enterprises that challenge established firms, disrupt the current ways of production and organization, and erode the competitive advantages of the established firms. A "deepening" or "creative accumulation" pattern of innovation is characterized by the dominance of a few large, established firms and barriers to entry to new innovators and entrepreneurs. In this case, innovations originate predominantly from the R&D activity of established firms and are based on accumulated stock of knowledge in specific technological areas and competencies in R&D built over time. A "creative destruction" dynamic may evolve into "creative accumulation" during the evolution of an industry (Breschi et al., 2000).

Sector: A set of activities that are unified by related product groups for a given or emerging demand and that share some basic knowledge (Malerba, 2005).

Sectoral system of innovation: Comprised of a set of heterogeneous agents (individuals such as scientists and entrepreneurs; and organizations such as firms, universities, government agencies, and financial institutions) involved in market and non-market interactions for the generation, adoption, and use of technologies and for the creation, production, and use of products that pertain to a sector (Malerba, 1999).

Single linkage: Distance between a point from one cluster and a point from another cluster that are closest to each other and that represents the minimum distance between

the two clusters.

Spillover: *Knowledge spillover* is the transfer of knowledge from one agent to another without compensation or compensation less than the value of the knowledge (e.g., through reverse engineering). *Market spillover* results when the operation of the market causes benefits to flow to market participants other than the innovating firm (e.g., when an innovative product is sold at a price that does not fully capture all of the superiority of the product, such that consumers are made better off). The effect of spillovers is to create a gap between the private rate of return from R&D (the profit earned by the firm that invested in the R&D) and the social rate of return, which includes both the private return and benefits to customers and to other firms.

Technological regime: A technological regime is defined by a combination of four key factors: 1) level and sources of technological opportunities (i.e., availability of external sources of knowledge), 2) conditions for appropriating the economic rents from innovation, 3) extent to which new technological advances build cumulatively upon past ones, and 4) nature of the knowledge base underpinning the innovation (i.e., basic science-based versus applied science-based) (Breschi et al., 2000). Sectoral patterns of innovation are based on the nature of different technological regimes. Innovative activities fall under the "widening" pattern when there is high level of technological opportunities, poor appropriability conditions, low level of cumulative knowledge required at the firm level, and limited role of knowledge base stemming from basic science work (described as more generic and less targeted knowledge) (Breschi et al.,

2000).

Technology: Structures, systems, and devices that help achieve predictable outcomes.

Transaction costs (with respect to alliances)**:** Costs of negotiating and writing contracts, enforcing contractual agreements, monitoring, and addressing contractual breeches.

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Appendix A: National Survey to Evaluation the NIH SBIR Program

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NATIONAL SURVEY TO EVALUATE THE NIH SBIR PROGRAM

The following award was identified through the National Institutes of Health (NIH) databases as a Small Business Innovation Research (SBIR) Phase II award. Please keep this particular award in mind when responding to the survey questions.

Company:	Principal Investigator:
Award Number:	Company Contact:
Project Period:	NIH Sponsoring Institute:
Project Title:	

SECTION A

The following questions ask for information about the company identified above that won the referenced SBIR award.

1. To the best of your knowledge, in what year was this company founded?

2. Which of the following best describes this company's major field of business?

(PLEASE SELECT ONLY ONE.)

□ Biotechnology
□ Pharmaceuticals
□ Diagnostics
□ Medical devices
□ Healthcare
□ Medical education, health promotion
□ Instrumentation
□ Computer hardware, software
□ Other (please specify): _____

3. If the SBIR program were not available, would the project funded by the referenced award still have been pursued?

□ YES
□ NO

□ NOT SURE / DON'T KNOW

4. Which one of the following most characterizes the product, process, or service that was planned under this project?

(PLEASE SELECT ONLY ONE.)

□ A totally new product, process, or service
□ An improvement to an existing product, process, or service
□ A combination of products, processes, or services
□ A new use for an existing product, process, or service
□ Other (please specify): _____

5. Has the company won any other SBIR Phase I or Phase II awards, in addition to the referenced award, for products, processes, or services that are related to this project? (The awards may have different principal investigators, and they may have come before or after the referenced SBIR award and from different NIH agencies.)

□ YES, then CONTINUE

□ NO or □ NOT SURE, then GO TO Q.8

6. How many SBIR Phase I awards, that involve products, processes, or services related to the project supported by the SBIR award referenced earlier, has the company won?

7. How many other SBIR Phase II awards, that involve products, processes, or services related to the project supported by the SBIR award referenced earlier, has the company won?

8. How important overall has SBIR support been, or how important will it be, in research and development of this product, process, or service?

□ Very important
□ Important
□ Somewhat important
□ Not important
□ Not very important

9. Did the granting of one or more SBIR awards for this product, process, or service have an impact on any of the following activities….

(PLEASE SELECT ONE RESPONSE FOR EACH ACTIVITY.)

	Yes	No	Not sure

Pursuing a high-risk idea or action that might not otherwise be undertaken			
Hiring additional personnel			
Raising additional capital			
Credibility or visibility for finding partners			

SECTION B

The following questions ask about commercialization of the product, process, or service resulting from the project supported by the referenced SBIR award.

10. When you applied for this SBIR award, what product, process, or service did you plan to commercialize?

(PLEASE SELECT ONLY THE ONE MOST APPROPRIATE CATEGORY.)

□ Drug
□ Device
□ Biologic
□ Genomic
□ Research tool
□ Software
□ Educational materials
□ Other (please specify):_____

11. Was or is FDA approval required for the product, process, or service selected above?

□ YES, then CONTINUE

□ NO, then GO TO Q.14

12. Has this product, process, or service been submitted for FDA review?

□ YES , then CONTINUE
□ NO, NOT YET, then GO TO Q.14

13. In what stage of the FDA approval process is this product, process, or service?

□ Applied for approval
□ Review ongoing
□ Approved
□ Not approved
□ Other (please specify): _____

14. Please give any applicable trade or commercial name, the generic name, and the model number for this product, process or service:

Trade or Commercial Name:

_____

Generic Name: _____

Model Number (if applicable):

_____

15. A. From the following list, please select the categories that best describe the medical, societal, or technological outcome(s) that relate to the product, process, or service supported by the above referenced SBIR award. (PLEASE SELECT ONLY APPROPRIATE OUTCOME(S).)

B. Next, select the single category that is the most important medical, societal, or technological outcome.

Q.15A: SELECT ONE OR MORE from "Outcomes" column

Q.15B: SELECT ONE from the "Most important outcome" column

	Outcomes	Most important outcome
Preventing disease or disability		
Detecting disease or disability		
Diagnosing disease or disability		
Treating disease or disability		
Reducing the cost of medical care		
Developing information for health care professionals		
Developing health information for the general public		
Fostering new research collaborations		
Improving research tools		
Training research investigators		
Other (please specify):		

16. A. From the following list, please select those population(s) who are currently using, or are likely to use, the product, process, or service developed under this project?

(PLEASE SELECT ONLY APPROPRIATE POPULATION(S).)

B. Next, select the single population that is the most important population.

Q.16A: SELECT ONE OR MORE from "Populations" column
Q.16B: SELECT ONE from the "Most important" column

	Populations	**Most important** population
Hospitals, patients:		
Outpatients		
Inpatients		
Hospital personnel		
Laboratories:		
Research laboratories		
Diagnostic laboratories		
Healthcare providers:		
Medical practitioners		
Homecare providers		
Emergency medical services		
Military medical services		
Other health services		
Other populations:		
General public		
Educators		
Worksites		
Schools, universities		
Police, fire, other municipal workers		
Other companies, other technologies		
Other (please specify):		

17. Within the next few years, what is the anticipated size of the total target populations that would benefit from or use the product, process, or service being developed under this project?

□ Under 10,000 persons
□ 10,000 – 49,999
□ 50,000 – 199,999
□ 200,000 – 499,999
□ 500,000 or more
□ Not sure

18. What is the current status of the project funded by the referenced SBIR award?

(PLEASE SELECT ONLY ONE.)

□ Under development or □ Commercialization stage or □ In use by target population then GO TO Q.20

□ Discontinued, then CONTINUE
□ Other (please specify):
_____, then GO TO Q. 20

19. Did the reasons for discontinuing this project include any of the following….

(PLEASE SELECT YES OR NO FOR EACH REASON.)

	Yes	No
Idea failed		
Market demand too small		
Level of risk too high		
Not enough funding		
Company shifted priorities		
Principal investigator left		
No FDA approval		
Licensed to another company		
Product, process, or service not competitive		
Other (please specify):		

► GO TO Q.24

20. Which of the following describes the status of marketing activities by your company and/or your licensee for this project….

(PLEASE SELECT ONE RESPONSE FOR EACH ACTIVITY.)

	Not yet planned	Planned	Ongoing	Complete	Need assistance	Not applicable
Preparation of marketing plan						
Hiring of marketing staff						
Publicity and advertising						
Test marketing						

SECTION C

The next group of questions asks about the economic impact of the product, process, or service resulting from the project supported by the SBIR award referenced earlier.

21. Upon completion of the project, were (or are) sales expected? (Include both sales and sales of licenses.)

□ YES , then CONTINUE

□ NO, then GO TO Q.24

22. With regard to sales, which of the following resulted?
(PLEASE SELECT ONLY ONE RESPONSE.)

□ Sales were realized , then CONTINUE
□ Sales are anticipated , then GO TO Q.24
□ Other (please specify): _____, then GO TO Q.24

23. What is the dollar range of cumulative sales related to the product, process, or service developed under this project?

□ $50,000 or less
□ $50,000 -$99,999
□ $100,000 -$499,999
□ $500,000 -$999,999
□ $1,000,000- $4,999,999

□ $ 5,000,000- $49,999,999
□ $50,000,000 or more

24. What is the current number of total employees (full-time equivalents) in your company?

SECTION D

The following questions ask about any additional funding that your company may have received for the project supported by the referenced SBIR award.

25. Has your company received any additional non-SBIR funding or capital for this project?

□ YES , then CONTINUE

□ NO, then GO TO Q.29

26. Do you believe that this additional funding or capital is a result of the NIH SBIR funding for the product, process, or service developed under this project?

□ YES
□ NO
□ NOT SURE

27. Thinking now about the sources of additional funding or capital for this project and its outcome (product, service, or process), were or are any of the following sources important?

(PLEASE SELECT YES OR NO FOR EACH SOURCE.)

Q.27: SELECT YES OR NO FOR EACH line in "Important sources" column
Q 28: SELECT one from the "Most important" column

	Important sources Yes	No	**Most important**
Non-SBIR federal funds			
Your own company			
Other private company			
U.S. venture capital institution			
Foreign venture capital institution			
Private individual investor			
Personal funds			

State or local government funds			
College or university			
Other (please specify): _____			

28. Which source has been or is the most important source of additional funding or capital? (PLEASE SELECT ONE from the RIGHTMOST "MOST IMPORTANT" COLUMN ABOVE.)

29. Which, if any, of the following has your company experienced because of the product, process, or service developed during this project?

(PLEASE SELECT YES, NO, OR NOT SURE FOR EACH ACTIVITY.)

	Yes	No	Not sure
Debt financing			
Private placement (angels, VC, relatives)			
Public offering			
Set up one or more spin-off companies			
Joint venture (academic or commercial)			
Sold company			
Merged company			
Licensed agreement			

►IF YES ON Q.29, PUBLIC OFFERING, CONTINUE. OTHERWISE GO TO Q.31.

30. A. On which stock exchange is your company listed?

□ New York Stock Exchange (NYSE)
□ NASDAQ
□ American Stock Exchange (AMEX)
□ Other (please specify): _____

B. What is its ticker symbol?

SECTION E

The next questions ask about possible contributions to the intellectual property and knowledge base resulting from support for this project by the SBIR award referenced earlier.

31. Which of the following items, associated with the product, process, or service developed under the project supported by the SBIR award referenced earlier, have you or your company received or achieved?

(PLEASE SELECT YES OR NO FOR EACH ITEM.)

Q.31: SELECT YES OR NO FOR EACH ITEM line in "You or company received or achieved" column
Q.32: GIVE THE NUMBER FOR EACH "YES" ITEM in the "Number" column

	You or company received or achieved Yes	No	**Number** received or achieved
Patents			
Copyrights			
Trademarks			
Publications in press or journals			
Conference presentations			
Awards (such as Tibbetts or state)			
Other (please specify):			

32. For each of the items above that you or your company received or achieved, please indicate how many items were received or achieved. (PLEASE USE THE RIGHTMOST "Number" COLUMN ABOVE.)

SECTION F

The last few questions ask about you and your experiences with the NIH SBIR award process.

33. Thinking now just about the referenced award, how satisfied were you with your experiences going through the SBIR application, review, and award process?

(PLEASE SELECT ONE IN EACH ROW.)

	Completely Satisfied	Mostly Satisfied	Mixed	Mostly Dissatisfied	Completely Dissatisfied	Not Applicable
Obtaining information about the SBIR program						
Instructions for preparing applications						
Review process						
Award process						
Post-award administration						
Other (please specify):						

34. Were you aware that you could contact NIH staff for additional information or assistance about any aspects of the SBIR grant review, award, and management process?

□ YES

□ NO

35. Based on your experiences with this and other SBIR awards, do you have any suggestions, comments, or criticisms to offer about both the strengths and weaknesses of the SBIR program? (Your advice will be valued greatly.)

36. Which of the following best describes your role in the SBIR award referenced earlier?

(PLEASE SELECT ONLY ONE.)

□ Initial principal investigator
□ Subsequent principal investigator
□ Other investigator
□ Company contact on SBIR application
□ Other company contact
□ Other (please specify): _____

37. Which of the following characterize your current relationship with this company?

(PLEASE SELECT YES OR NO FOR EACH RELATIONSHIP.)

	Yes	No
An employee		
An owner		
Part of management		
A shareholder		
Other (please specify):		

38. How well do you feel you were able to recall the information that this survey requested about the referenced SBIR award?

□ Very well
□ Well
□ Somewhat well
□ Not well
□ Not very well

Appendix B: Classification of university/basic partners versus clinical partners.

Clinical Disciplines	Basic Disciplines
Anesthesiology	Anatomy
Biostatistics	Bacteriology
Epidemiology	Biochemistry
Gastroenterology	Cancer biology
Geriatrics	Cell biology
Hematology	Chemistry
Internal medicine	Cytology
Medicine	Embryology
Nephrology	Endocrinology
Neurology	Genetics
Obstetrics and Gynecology	Histology
Oncology (but not "cellular" oncology)	Immunology (unless specified as "clinical" immunology)
Ophthalmology	Infectious diseases
Particular disease name, e.g., diabetes	Microbiology
Pathology	Molecular biology
Pediatrics	Neurosciences
Periodontics	Nutrition
Psychiatry	Parasitology
Radiology	Pathobiology
Rheumatology	Pharmacology (unless specified as "clinical" pharmacology)
Surgery	Physiology
Therapeutics	Psychology
Transplantation	Toxicology
Urology	
Specific diseases (e.g., Diabetes)	

Appendix C: Logistic regression analysis of interaction between firm age and interfirm partnerships on innovation success, controlling for FDA.

Dependent variable is INNOV, where innovation success includes having the product currently in use by target population or in the commercialization stage

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AgeStartUpR	.303	.476	.406	1	.524	1.354
	FIRMA	.621	.307	4.097	1	.043	1.860
	CLINA	-.046	.033	1.933	1	.164	.955
	UNIVA	.041	.041	1.011	1	.315	1.042
	AgeStartUpR by FIRMA	-.560	.298	3.528	1	.060	.571
	FDA	-2.070	.318	42.279	1	.000	.126
	Constant	.355	.442	.643	1	.422	1.426

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	241.310	.244	.327

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AgeStartUpR	.462	.563	.672	1	.412	1.587
	FIRM	1.894	.765	6.128	1	.013	6.647
	CLIN	-.032	.381	.007	1	.933	.969
	UNIV	.176	.431	.167	1	.683	1.192
	AgeStartUpR by FIRM	-1.538	.811	3.599	1	.058	.215
	FDA	-2.189	.329	44.142	1	.000	.112
	Constant	.066	.519	.016	1	.899	1.068

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AgeStartUp	-.462	.563	.672	1	.412	.630
	FIRM	.356	.408	.762	1	.383	1.428
	CLIN	-.032	.381	.007	1	.933	.969
	UNIV	.176	.431	.167	1	.683	1.192
	AgeStartUp by FIRM	1.538	.811	3.599	1	.058	4.656
	FDA	-2.189	.329	44.142	1	.000	.112
	Constant	.528	.383	1.900	1	.168	1.695

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	241.257	.244	.327

Appendix D: Logistic regression analysis of the effect of big firm partners on innovation success, controlling for FDA.

Dependent variable is INNOV, where innovation success includes having the product currently in use by target population or in the commercialization stage

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	.020	.030	.455	1	.500	1.021
	BIGFIRM	.757	.354	4.565	1	.033	2.132
	CLIN	-.044	.370	.014	1	.905	.957
	UNIV	.260	.407	.410	1	.522	1.297
	FDA	-2.182	.327	44.573	1	.000	.113
	Constant	.303	.383	.628	1	.428	1.354

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	243.504(a)	.236	.317

Appendix E: Logistic regression analysis of alliances with different types of partners in start-up population.

Dependent variable is INNOV, where innovation success includes having the product currently in use by target population or in the commercialization stage.

A. Number of alliances with firm, university, or clinic partners as determinant of innovation success

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	-.088	.337	.069	1	.794	.916
	FIRMA	.821	.421	3.805	1	.051	2.273
	CLINA	-.160	.095	2.872	1	.090	.852
	UNIVA	.052	.098	.284	1	.594	1.053
	Constant	-.348	.824	.178	1	.673	.706

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	53.941(a)	.212	.283

B. Number of alliances with firm, university, or clinic partners as determinant of innovation success, controlling for FDA

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	-.466	.459	1.032	1	.310	.627
	FIRMA	1.007	.534	3.552	1	.059	2.736
	CLINA	-.073	.111	.436	1	.509	.930
	UNIVA	-.023	.124	.033	1	.855	.978
	FDA	-3.348	1.000	11.217	1	.001	.035
	Constant	1.904	1.251	2.315	1	.128	6.710

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	37.098(a)	.449	.599

Appendix F: Logistic regression analysis of alliances with different types of partners in older firm population.

Population of firms that had been founded 4 or more years prior to the SBIR award.

Dependent variable is INNOV, where innovation success includes having the product currently in use by target population or in the commercialization stage.

A. Number of alliances with firm, university, or clinic partners as determinant of innovation success

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	.023	.030	.604	1	.437	1.023
	FIRMA	.055	.064	.719	1	.396	1.056
	CLINA	-.047	.030	2.378	1	.123	.955
	UNIVA	.042	.038	1.215	1	.270	1.043
	Constant	-.611	.332	3.392	1	.065	.543

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	236.343(a)	.024	.033

B. Number of alliances with firm, university, or clinic partners as determinant of innovation success, controlling for FDA

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1	AGE	.033	.034	.930	1	.335	1.033
	FIRMA	.042	.072	.342	1	.559	1.043
	CLINA	-.037	.034	1.170	1	.279	.964
	UNIVA	.046	.044	1.117	1	.290	1.047
	FDA	-1.945	.347	31.452	1	.000	.143
	Constant	.303	.397	.582	1	.445	1.354

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	201.077(a)	.202	.271