University of California,
Irvine

# **An Emergence of a Biotechnology Cluster**:
Knowledge, Practice and Culture of the San Diego Biotechnology Community

**DISSERTATION**

Submitted in partial satisfaction of the requirements of the degree of

DOCTOR OF PHILOSOPHY

in Planning, Policy and Design

by

Kim, Sang-Tae

**Dissertation Committee:**

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2011

# DEDICATION

To my brother Sang-Sik,

Who filled my heart and soul with wonder and love.

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# ACKNOWLEDGMENTS

Like any human endeavor, this research was an incremental, iterative and interactive process, which involved many people's insights and inputs.

This research project was harder and longer than I had expected. I often became anxious and exhausted in the process. What kept me moving and moving were my interviewees and fieldtrips to San Diego. Whenever I got into my car and on the way to San Diego, either for an interview or a field observation, I gained a new stream of motivation and energy to move forward. Every interview made a big difference for this dissertation, and, indeed, me. Still, I cannot believe the kind of people I interviewed and with whom I interacted. In my case, they not only gave information that constitutes the body of this research, but they also impressed and inspired me to continue this journey. What I gained from every interview was not only data, but truly invaluable mentoring, advice and encouragement that will stay throughout my life. I will never forget every moment and every account with my interviewees. My heart will be with the San Diego community for a long time. My interviewees, you are truly my mentors. Thank you!

I could not believe how much support I had from my adviser and committee. I am not able to describe the support I have received from my academic advisers appropriately. At interviews, many entrepreneurs told me there is nothing more important than having extraordinary mentors and advisers around them. They emphasized the power of such communities in overcoming difficulties and continuing entrepreneurial endeavors. I, personally, have experienced the power of a supporting community in the process of interacting with my adviser and committee members. Knowing that my adviser, Scott Bollens, would read whatever I wrote and give the advice of the best scholar has been instrumental to completing this dissertation. He taught me to write better and to think more, which I have to practice throughout my career. Scott is my role model. I want to be a scholar or a practitioner like Scott. He is ready to go to any city in conflicts, and he comes back with a lot of sympathy and excitement. I learned from Scott what makes our life valuable and memorable: devotion to students and commitment to our work.

Without Martha Feldman, I would have never reached this point. She is more than an advisor, teacher or supporter; Martha was a magician. Frustrated and disheartened, I always leaned on Martha. A talk with her for ten minutes or one hour, and a hug changed everything. After coming back to my office, I found myself engrossed in the joy of learning. One time, I came to her and complained about the anxiety and hardship involved in living as a researcher, who is constantly harassed and frustrated by inquiries. I continued to say that I would rather find a job having no such anxiety and stress. Listening to me, she asked me to inform her if I could find such a job, so she could leave her professorship to work there. Even though the job is hard to live, she said, "we, now, could take a shower every day." From that moment on, every shower at night became a special ritual to me: it is the best reward from everyday work.

Yan Gong has been very special to me. I don't know why he supported me during the last two years. He was concerned about my financial situation and my family. I still clearly remember a field trip to San Diego together with Yan. On the way to and back from San Diego, we talked a lot about developing countries: Korean and China, which have been struggling to catch up the developed countries, but still have a long and bumpy way to go. Yan was always collegial and passionate.

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I am always thankful to my family. My wife, Hyo-Seon, has been an incredible listener. At this point, I am sorry for having kept you listening to my interests, inspirations and ideas related to my research virtually every day. It was the conversations with Hyo-Seon that turned any emerging ideas into logics and concepts. My sons, Jeong-Yup and Kevin, have always given me the cause for learning and living. Finally, I am greatly indebted to my brother, Sang-Sik and my sister-in-law, Sun-Hee Choi. I don't know how my brother educated me from middle school to college, as a father of two children. What’s more, he opened my eyes and ears to the social sciences by telling and reading to me great ideas. He brought to me the wonder of the social world by educating and loving.

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Dissertation:

"**An emergence of a biotechnology cluster: Knowledge, practice and culture of the San Diego biotechnology community**." This dissertation explores how a biotechnology cluster and relationships between academia-industry in San Diego have been constructed. It is based on in-person interviews, field observations and extensive archives. This study suggests that localization of industry and knowledge transfer should be understood as process of learning in communities of practice. Participants have developed knowledge and practices in the process of acting and interacting to deal with daily problems and issues in communities of practice. The local knowledge, practices and shared understanding built on daily interactions account for robust entrepreneurial activity and academia-industry collaboration in San Diego. This dissertation was supervised by dissertation chair Scott A. Bollens and supported by dissertation committee members Martha S. Feldman and Yan Gong.

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# ABSTRACT OF THE DISSERTATION

An emergence of a biotechnology cluster:

Knowledge, practice and culture of the San Diego biotechnology community

By Sang-Tae Kim

Doctor of Philosophy in Planning, Policy and Design

University of California, Irvine (2011)

Professor Scott A. Bollens (Chair)

The biotechnology industry in San Diego started to emerge in the 1980s, and by the 2000s, it became one of the most dynamic biotechnology hubs in the country. It consists of hundreds of public and private companies; a set of renowned research institutions, including the University of California, San Diego; and a group of specialized practitioners. San Diego is also recognized for a number of successful partnership programs and a culture of collaboration. Pertaining to the San Diego biotechnology community, I raise the following questions: *which factors stimulate entrepreneurship; how have these factors been constructed; and what enable or constrain technology transfer from academia to industries.* In analyzing data and constructing theoretical concepts, I was guided by 'grounded theory' and interpretivist approaches.

Lacking any industrial tradition and infrastructure, the San Diego region employed talent, practices and resources from outside. By working at small biotechnology companies, managers and employees started to develop expertise on technologies and management as well as to create relationships with each other. Communities, where

groups of people interact to solve problems and issues together, have been the locus of learning and becoming. Through their daily practices and involvement in communities, many individuals have become skillful entrepreneurs or entrepreneurial scientists. It is the daily social interactions and interpretations, which have fueled entrepreneurship and technology transfer of this biotechnology community. Biotechnology companies, research institutions and specialized service providers have agglomerated around the University of California, San Diego, thus individuals and organizations had frequent face-to-face interactions across communities as well as in communities. To tackle issues in common, the community embarked on a series of collective actions, which contributed to building shared understanding and memories. These experiences and engagements under the leadership of trade associations and research institutions have been critical to creating a culture of collaboration. A culture of collaboration has been the key to expanding and energizing this network of entrepreneurs. In sum, it is learning and experiencing in communities, which have produced the talent and resources for entrepreneurship, and it is interactions and engagements at the entire community level that have given San Diego a competitive edge.

# CHAPTER 1: INTRODUCTION

‘Localization’ of industries, which is coined as ‘clusters,’ ‘technopoles,’ ‘science parks,’ or ‘industrial districts,’ is a fascinating social and economic phenomenon to researchers and policy makers. In the modern period, regions like Silicon Valley, Route 128 and Southern California have been the locus of innovation and entrepreneurial activity around high-technology and biotechnology industries. Silicon Valley is not only recognized as a hub of computer and information industries, but regarded as the best case of entrepreneurial ecosystem. After decades of research, survey and observations, people around the world come to these clusters, partly hoping to nurture an entrepreneurial ecosystem in their home land and, partly, curious about the keys to prosperity. The resurgence of the U.S. economy in the last few decades is generally attributed to the rise of novel innovations, institutions and culture from these regions. According to a large body of literature on industrial clusters, these regions have some common characteristics: vibrant start-up activity, intimate interactions between industry and academia, dynamic learning process and collaborative culture. Moreover, in industrial clusters, there have emerged institutions and cultures that encourage and enable individuals to engage in experiments and interactions.

The robustness of entrepreneurial activity and industry-academia collaborations draws much attention from not only scholars but also policy makers at national, regional and city governments, many of whom continue to visit regions like Silicon Valley, Route 128 and San Diego, to figure out the regions' engine of economic expansion and excitement.

Until the 1980s, researchers and policy practitioners mostly focused on verifying and exploiting any given advantages generated by natural resources, geographical locations or cultural traditions. Regional sciences and analytical methods provided the platform for researchers to specify and suggest patterns and profiles of cities, regions and countries. Commonly, it was a single skill set and one sector which drew policy attention as an engine of regional economy. Therefore, polices revolved around providing favors to selected industries in the form of regulations and resources. Porter (1990) and his 'diamond theory' shifted the focus from an isolated, salient sector to interdependency of multiple factors at industrial clusters. Since the 1990s, research and remedies on urban, regional and national economy paid attention to the 'four-determinants’ of competitiveness and engendering business environment built on four components: (1) factor conditions; (2) demand conditions; (3) related and supporting industries; and (4) firm strategy, structure and rivalry. In many cases, the answers and remedies were to supplement or strengthen weak components of the diamond theory. Saxenian's (1994) study comparing Silicon Valley and Route 128, and Florida's (2002) emphasis on three Ts – technology, talent and tolerance – shifted interest to social aspects of entrepreneurship and innovation. These studies suggested that a regional economy could be understood as an ecology, industrial system or organic entity having a unique set of shared understanding and institutions.

Economists devised and drew on earlier concepts like externalities and agglomeration effects to explain the clustering phenomenon. In the late 19th century, Marshall (1961[1890]) attributed spatial agglomerations of interrelated companies to economic

externalities and the spread of ideas. External economies provided the basis for Porter (1990) to develop his 'diamond theory.' On one hand, studies from economics have contributed to verifying dynamics of industrial clusters. However, on the other hand, they could do no more than point to historical accidents or natural environment in explaining the genesis of clusters. There is also such a limitation in a series of empirical studies looking at the impact of research universities and academic scientists on generating and growing adjacent industrial clusters. Researchers and policy makers have found that any dynamic industrial clusters have links with neighboring research universities. The emergence of Silicon Valley is, at least in part, attributable to the research capability of Stanford University and the activity of its provost, Frederick Terman, while the revival of Route 128 – and, to some extent, the resurgence of Massachusetts economy – is traced to the efforts and engagements of Massachusetts Institute of Technology (MIT) and Harvard University. Increasingly, the literature and policy makers agree that research universities and academic scientists are indispensible elements for creating industrial clusters.
Still, however, the previous studies provide only a partial picture of the situation: some studies look into macro-level impacts or institutions, while others focus only on effect and efforts of pioneers.

I seek, in this dissertation, to understand the causes of robust entrepreneurship and of dynamic academia-industry collaboration at industrial clusters. Furthermore, I explore the historical process of ‘localization’ – the constitution of resources, institutions and culture of industrial clusters. I investigate the biotechnology community of San Diego and the constellation of entrepreneurs, investors, specialized service providers, academic scientists, public officials of local governments and representatives of trade associations. I look into the patterns and contexts of entrepreneurship and academia-industry interactions.

I raise two questions related to causes of entrepreneurial activity and origins of an entrepreneurial system:

1. *What enhances the vibrancy of biotechnology start-up activity in San Diego?*
2. *How has the entrepreneurial system been produced?*

I ask the following questions regarding the interactions between the local research institutions and industry:

1. *What factors facilitate or constrain interactions between academia and industry?*
2. *How have the factors which forge patterns of interactions between research institutions and industry been developed?*

I was intrigued by the growth of the biotechnology industry in San Diego, which started to draw attention as recently as the late 1980s or early 1990s, and has since grown to be one of the most dynamic and vibrant biotechnology clusters. San Diego used to be a 'sleepy navy town,' which lacked a significant base of innovation or tradition of technology entrepreneurship until the 1980s. San Diego was also called the cul-de-sac of California, which referred to the geographic and economic isolation of this region from the main part of the country until the last few decades. San Diego is still an isolated territory geographically: an international boarder to south, a military base (Pendleton) to north, the Pacific Ocean to west and a desert mountain (Anza-Borrego Desert) to east. San Diego also lacked any material or financial resources necessary to launch heavy industries, as well as any significant tradition to develop manufacturing industries. Until the 1980s, the most important parts of the local economy were military and tourism. The regional economy that had proliferated and prospered based, largely, on the expansion of federal spending on military, began staggering when the federal government cut its defense budgets in the mid-1980s.

The region recovered from its worst economic downturn in the modern decades by stimulating start-up entrepreneurship and supporting small local companies by the early 1990s. Leaders and practitioners have focused on creating a community that has enabled and encouraged individuals to venture into technology start-ups. There are several hundred life sciences companies, dozens of research institutions, including UCSD, and a group of specialized practitioners. The region also hosts a number of notable partnership programs and a culture of collaboration. Groups of delegates, not only across this country but from around the globe, visit San Diego to learn about the ingredients of its economic transformation. CONNECT, which was founded in 1985 to promote commercialization of academic research by UCSD, has been the benchmark for 41 similar programs around the world (Global CONNECT, 2010). In 2010, CONNECT received the Innovation in Economic Development Awards by the U.S. Economic Development Administration (EDA) under the category of 'Innovation in Regional Innovation Clusters'.

The biotechnology industry, institutions and resources emerged no earlier than the 1980s. Virtually no activity or facility of biomedical research existed until 1960. A research university, UCSD, and non-profit research institutions emerged on deserted military bases in La Jolla during the 1960s. This was a time when a number of research universities had already risen intellectually, based on policies of the federal government. A plan to establish a campus of the University of California in La Jolla was approved by its regents in 1959. Jonas Salk, the developer of polio vaccine, began building the Salk Institute for Biological Studies (the Salk Institute) next to UCSD in 1960. And a local clinic, the Scripps Clinic, opened a department for studying pathology in 1961. During the 1970s and 1980s, several more non-profit research institutions emerged around UCSD. To date, these research institutions together have become an anchor of federal research grants – in 2009 about $800 million of the National Institutes of Health (NIH) research funding flowed to San Diego, which accounted for 2.7 percent of the total NIH appropriations. Spatially, most biotechnology companies in San Diego are within walking or short driving distance from these research institutions. Historically, a majority of biotechnology companies were founded by scientists at these research institutions in efforts to commercialize research discoveries.

From a theoretical perspective, I draw on literature from multiple disciplines. Studies from economics, economic geography and regional planning have contributed to expanding our understanding on the proliferation and significance of industrial clusters. These studies have been instrumental in deepening and widening interests and insights. The literature has increasingly emphasized industrial clusters more as an ecosystem or a living organism, paying more attention to the dynamic interactions between multiple players and learning process at industrial clusters. Alternative literature looks at social and cultural aspects of entrepreneurship and innovation to explain the characteristics and capabilities of localized industrial systems. However, the literature sheds little light on the process or progress of 'localization'. I draw on structuration theory by Giddens (1979; 1984) and studies on organizations and social structures to look into the formation of rules and resources at the San Diego biotechnology cluster. I stand on studies of 'situated learning' and 'communities of practice' to understand localization, by looking at the experiences and efforts of individuals. Thus, this study broadens the literature on structuration and learning by applying the theories to exploring a formation of a biotechnology cluster and a pattern of academia-industry interactions.

San Diego is widely acclaimed as a case of restructuring itself to be a powerhouse of biotechnology and high-technology industries. Recently, San Diego and CONNECT were featured in Time magazine (Katz, 2010) as a case for reinvigorating national and metropolitan economies. The efforts to nurture the biotechnology industry have been mostly led by the local leaders in conjunction with entrepreneurs. The approach has been to cultivate start-ups locally and to foster academia-industry collaborations, rather than to attract large companies or to invest heavily in infrastructure. This case can provide lessons and guidelines to regions and cities around the country, which are in need of creating jobs and stimulating economic activity by cultivating and leveraging entrepreneurship more than ever. Around the globe, this case can provide a framework for public policies targeting biotechnology industry or regional clusters. At the same time, this research is meaningful to policy makers or practitioners who seek to leverage research capacities at universities to promote economic prosperity.

In exploring and explaining the emergence of a biotechnology cluster in San Diego and the formation of academia-industry relationship, I will proceed as follows. In Chapter 2, I will review the literature on industrial clusters and the role of research universities in nurturing local technology-based industries. To understand the role and formation of social structures on industrial localization and academia-industry collaboration, I will look at the literature on the theory of structuration and practice. Also, I will review studies on the role of social structures on economic development. In Chapter 3, I will describe how I have collected and analyzed the data drawing on grounded theory. In Chapter 4, I will present the historical development of the local community from the $19^{th}$ century to the 1980s. I will focus on the evolution of local economic base, the development of research institutions, land-use planning around UCSD, the beginning of local biotechnology industry and the communal efforts to nurture the biotechnology cluster. In Chapters 5 and 6, I will explore the research questions by looking at individuals' experiences and their institutional contexts. At the end of each chapter, I will provide concepts to answer the research questions. In the concluding chapter, I will briefly overview the implications of this research for the literature and policy.

# CHAPTER 2: LITERATURE REVIEW

To explore and explain the constitutive process of San Diego biotechnology cluster and the role of local research institutions, the literature review starts with studies on industrial clusters and technology transfer. The composition of previous studies on industrial clusters reveals that the social process is the primary ingredient of entrepreneurial activity. In industrial clusters, the robustness of entrepreneurial activity and innovation is sustained and expanded through collaborations and interactions between participants. In explaining knowledge transfer, the literature argues that the role and impact of research universities in constructing industrial clusters depend on organizational and social contexts. The extent of knowledge transfer between academia and industry, and entrepreneurial activity of faculty are contingent on social contexts including social relationships, interactions and attitudes toward entrepreneurship. While the literature suggests that social structures underlie the entrepreneurial activity both in industrial clusters and at research institutions, it provides limited insights into the link between social structures and entrepreneurial activity. Moreover, it does not account for the constructive process of social structures, which ultimately defines the development of industrial clusters and the role of research universities. To explore the nexus of social structures and economic activity, studies from economic sociologists as well as Schumpeter and Jacobs will be reviewed. I draw on theory of structuration and learning as a way to understand the constitutive process of social structures of the San Diego biotechnology community. Put together, the literature review seeks to provide theoretical frameworks guiding this research on how academics and academic research institutions are involved in economic activity as well as how a biotechnology community works, and how it is constituted, and how it has developed.

## 2-1. Industrial Districts: Ingredients and Development

The theories of industrial districts provide valuable insights into the context that is contingent on the development and sustainment of industrial clusters and the role of research universities in the process. Marshall's (1961[1890]) concept of industrial districts has been the most influential theory in forming the trajectory of subsequent research. Marshall (1961[1890]) intended to explain the underlying economic principles of a spatial agglomeration of interrelated companies, which he witnessed in late 19th century in Europe and the U.K. He called this phenomenon 'the localization of industry.' He (1961[1890], p. 268) gave an interesting case of a localized industry:

> Not very long ago travelers in western Tyrol could find a strange and characteristic relic of this habit in a village called Imst. *The villagers had somewhat acquired a special art in breeding canaries:* and their young men started for a tour to distant parts of Europe each with about fifty small cages hung from a pole over his shoulder, and walked on till they had sold all. (emphasis added)

With regard to the causes of the localization of industry, Marshall identified three factors: natural advantages, political leadership and historical events. So, in Marshall's account, the genesis of localized industries lies in the confluence of the natural environment, market demands for certain goods by the rich people, and social and political institutions. Marshall (1961[1890], p. 271) portrayed the process of expansion and proliferation as follows:

> When an industry has thus chosen a locality for itself, it is likely to stay there long: so great are the advantages which people following the same skilled trade get from near neighborhood to one another. *The mysteries of the trade become no mysteries; but are as it were in the air, and children learn many of them unconsciously*. Good work is rightly appreciated, inventions and improvements in machinery, in processes and the general organization of the business have their merits promptly discussed: if one man starts a new idea, it is taken up by others and combined with suggestions of their own; and thus it becomes the source of further new ideas. And presently subsidiary trades grow up in the neighborhood, supplying it with implements and materials, organizing its traffic, and in many ways conducing to the economy of its material. (emphasis added)

In this account, he clearly refers to the learning process through interactions and mutual engagements as the source of momentum for industrial districts. The second advantage comes from the development of subsidiary industries, which enable the localized firms to employ superior business services and materials at lower cost. Third, even though it is not mentioned in the above account, the formation of a large skilled labor market gives a competitive edge to localized industries and companies since laborers with special skills tend to congregate in places where the demand for their specialized labors is substantial. Therefore, firms in industrial districts can employ and lay off skilled employees without much cost, as the workers can also easily switch their workplaces.

One century later, Porter (1990; 2000) and Krugman (1991) draw largely on Marshall's concept of 'external economies' – which Marshall (1961[1890], p. 266) defined as the economies that are "dependent on the general development of the industry," referring to the economic benefits coming from external environment, not through market transactions – in explaining the industrial agglomerations from the perspective of management and economics. Porter broadens Marshall's idea to explain the divergent economic competitiveness between regions, and suggested industrial strategies focusing on the external environment of companies, which is widely known as the ‘diamond model’. In his definition, regional clusters are vertically or horizontally interconnected industries located in a certain geographical area where local companies benefit from linked industries and interrelated firms.

Porter (2000) suggests two economic underpinnings of the formation and proliferation of industrial districts: static economic gain originating from diminished costs of employing business resources; and dynamic, long-term advantages resulting from increased competition, as well as localized knowledge spillovers, and creation of functional institutions, which are all interwoven to stimulate innovation. Among these external economies, localized knowledge spillovers take place as firms in an industrial cluster are “exposed to richer insights into evolving technology, component and machinery availability, service and marketing concepts, and the like” (Porter, 2000, p. 23), so it encourages local firms to venture into new dimensions of the technology and market. As a whole, in Porter’s (1990, p. 151) words, “the presence of the cluster helps increase information flow, the likelihood of new approaches, and new entry from spin-offs, downstream, upstream, and related industries." Krugman (1991) also points to external economies and cumulative processes as the causes of industrial agglomeration. As soon as there emerges robust industrial activity in a certain region, relevant firms tend to congregate in this geographical area to take advantage of economies of scale.

Many researchers have been fascinated with cases of local clusters such as Silicon Valley, Route 128 around Boston, Southern California, and the Research Triangle Park in North Carolina, to name a few. It is meaningful to examine studies on these cases as each of the studies gives some clues about process and mechanism of localization in each local context. In this regard, the literature on Silicon Valley and renowned high-tech regions has significant implications for understanding the genesis and development of industrial localizations. The study by Saxenian (1994) is significant in that she reoriented research focuses to cultural and social dimensions from impacts of economic externalities. In the comparative case study on Silicon Valley and Route 128, she discovered different types of practices between these two regions. The network-based industrial system in Silicon Valley has facilitated innovation and entrepreneurship through knowledge sharing across companies and entrepreneurs, whereas the vertically integrated corporate structures and its autarkic culture in the Boston area have constrained local companies from adapting to the changing technological, market environment. Therefore, the practices embedded in the regional culture and social ties in Silicon Valley have critical to promoting entrepreneurship. In her (1994, p. 2-3) account:

> Silicon Valley has a regional network-based industrial system that promotes collective learning and flexible adjustment among specialist producers of a complex of related technologies. The region's dense social networks and open labor markets encourage experimentation and entrepreneurship. Companies compete intensely while at the same time learning from one another about changing markets and technologies through informal communication and collaborative practices; and loosely linked team structures encourage horizontal communication among firm divisions and with outside supplies and customers. The functional boundaries between firms are porous in a network system, as are the boundaries between firms themselves and between firms and local institutions such as trade associations and universities.

This perspective resonates with Lee, Miller, Hancock and Rowen's (2000) definition of Silicon Valley, 'local clusters of knowledge and relationships'. In their argument, tight links between members of entrepreneurial ecology, including entrepreneurs, investors, universities and other participants, promote the flow and accumulation of knowledge, and facilitate interactions and collaborations. In conclusion, they (p. 15) argued that Silicon Valley is where "a practiced and creative process among people networked within a habitat, the cumulative product of much trial and error and learning over time" take place. Brown and Duguid (2000a) claimed the robust generation, circulation and utilization of the 'mysteries of the trade' in the industrial clusters, particularly Silicon Valley, are rooted in communal practice and interactions. Knowledge is created and circulates among individuals having shared experience, meanings and goals. Without experience of practice and face-to-face interactions, the ability of recognizing and exploiting 'mysteries' in the air should be limited. In the industrial clusters, the geographic proximity and density of social networks allow members to participate in practices of community through face-to-face interactions.

These views focus on the dynamics of knowledge and networks in Silicon Valley. Individuals in the Valley are able to recognize the next 'big things' and to turn the ideas and insights into products earlier than people in any other regions because they are linked to each other and to informants around the world. They are more capable of exploiting their stock of technological and market knowledge into a new venture. So, people with ideas, skills and passion around the country and overseas prefer to come to Silicon Valley and other high technology centers because they can access the necessary expertise and resources.

While Saxenian (1994) (regional network-based industrial system), Lee et al. (2000), (local clusters of knowledge and relationships) and Brown and Duguid (2000) (networks of practice) employ networks or local clusters to explain the dynamics of Silicon Valley, other scholars draw on somewhat different concepts to explain the entrepreneurial dynamism. For example, Cohen and Fields (1999) employ the concept of 'social capital' as the enabler of robust collaborations and interactions between regional players. In their explanation, social structures and institutions in Silicon Valley have evolved to stimulate and sustain interactions and collaborations, which, in turn, have forged the innovative networks. In a study of ‘technopoles’ across the globe, Castells and Hall (1994) point to 'creation of synergy' as the source of regional competitiveness and advantage in industrial districts. By creation of synergy, they (p. 224) mean "the generation of new and valuable information through human interaction." Since human interaction is mediated by social institutions and networks, they (p. 234) concluded that "without an innovative local society, supported by adequate professional organizations and public institutions, there will be no innovative milieu." Florida (2002) draws further attention to the critical role of places in attracting and stimulating 'creative class'. Human creativity thrives in places where people have rich, diverse and dynamic experiences from interactions within social, cultural and natural environment. The 'creative class' moves to and settles down in places that reflect and reinforce their identities as 'creative people'. In this sense, the localities fitting with the creative class become the hub of innovation, firm formation and firm growth.

Some researchers focus on the supportive business environment for start-ups. Kenney and von Burg (2000) looked at the systems and institutions dedicated to nurturing and promoting new businesses. They divide the institutional arrangements in Silicon Valley into two categories: 'Economy One,' which mainly consists of established firms and research institutions; and 'Economy Two,' which is dedicated to nurturing start-ups. The Economic Two is "the institutional complex specialized at creating new firms aimed at exploiting fast-moving technological trajectories," according to Kenney and von Burg (2000, p. 222), which are embedded in Silicon Valley as routine and practice. Bahrami and Evans (2000) also focus on institutions for supporting start-ups. They argue that Silicon Valley should be understood as an 'ecosystem' that provides a supportive environment for nurturing start-ups through the 'process of flexible recycling'. In this view, social institutions fuel the region to create a series of start-ups, which embody novel ideas and capacities in propelling innovation.

The studies from economics and management give a primary focus on the existence of external economies and the factors generating externalities, while perspectives from sociology and urban studies draw more attentions to the social and cultural structures of industrial clusters. Studies from economics provide rich empirical evidence on the existence of agglomeration effects, but they provide limited insights into the emergence and development of industrial districts and also little explanation on the underlying sources of dynamism. In explaining the formation of industrial clusters, Porter (1990, p. 163-4) wrote:

> The seed of a competitive industry may have been sown by chance. Or other nations may have been in a similar position initially. From there, though, the process of building a competitive industry takes on a momentum of its own. This momentum, fueled by the widening and self-reinforcement of the determinants, moves the industry toward broader and more robust advantages.

Krugman (1991, p. 64) also attributes the emergence of localized industries to historical coincidence or leadership of individuals. He wrote:

> Silicon Valley was created by largely through the initiative of Fred Terman, the vice-president of Stanford University… Route 128 was created, in a more diffuse way, through the initiative of MIT's president, Karl Compton, who encouraged MIT faculty to become entrepreneurs and helped mobilize private venture capital. North Carolina's Research Triangle, finally, was created through state support of a research park, in direct emulation of Silicon Valley and Route 128.

By virtue of these historical accidents or personal endeavors, a substantial number of companies and related organizations agglomerate at a certain region or city. Then the increasing returns from clustering attract more entrepreneurs further enhancing the external economies of location.

Saxenian's (1994; 2000; 2004) studies provide insight into the growth of culture and practice in Silicon Valley and the Hsinchu IT cluster in Taiwan. Saxenian (1994) attributed the formation of production models in Silicon Valley to the entrepreneurial pioneers who worked under the early cultural and geographic context of this region: freedom from conventional norms and geographic proximity between enterprises. During the decades of 1970s and 1980s, the creative reactions by high-technology companies and entrepreneurs to the rapidly changing markets and technological environment shaped an idiosyncratic culture and organizational forms in this region. Furthermore, in a study of Hsinchu IT cluster, Saxenian (2004, p 194) coined the concept of “entrepreneurship-led growth” to capture the dynamics generated through collaborations and competition among small enterprises and start-up entrepreneurs. It was the Taiwanese technologists and entrepreneurs from Silicon Valley and public research institutions who changed the low-cost and low-value-added information and technology (IT) industries into the most technologically advanced one through ‘learning by doing’ and rigorous experimentations for new protocols.

In tracing the historical germination and evolution of three key companies in Silicon Valley – Eitel-McCullough, Varian Associates and Fairchild Semiconductor – Lecuyer (1999) also concludes that the builder of the valley was a group of entrepreneurs and technologists, who shaped a culture and practice of innovation. Therefore, in Lecuyer’s (p. 7) words, “the Peninsula’s electronics manufacturing complex should be seen as a continually shifting ecology of machines, skills, practices, technical groups, and institutions which were embedded in a unique social and economic environment, the San Francisco Bay Area.” In his reflection over the emergence of Silicon Valley, Moore (Moore & Davis, 2004), the inventor of Moore’s law and the cofounder of Intel, contended that it was the 'Fairchild University' that had created the structures and culture of the valley. The technological breakthroughs and the ‘Silicon Valley-defining modes of business,’ according to him, were the product of ‘technologist-managers.’

The Research Triangle Park in North Carolina also has drawn attention from scholars and policy practitioners, since it is generally regarded as an illuminating case of a 'man-made' cluster. It has become one of the most energetic high-technology clusters made from scratch. It was articulately designed and managed by pioneers with an intention of transforming one of the poorest states into a hub of innovation during the 1950s. The research park is in proximity to three research universities – Duke University, the University of North Carolina at Chapel Hill and North Carolina State University – and a number of renowned research institutions including an IBM research facility. Link (2002) attributed the success of this industrial park to two ingredients: the vision and commitment of leaders, who tailored infrastructure for industries and created institutions to leverage the potential; and outstanding universities and research institutions. The efforts were led by two institutions: TUCASI (the Triangle University Center for Advanced Studies) took the role of promoting joint research and education between the three universities; and the North Carolina Biotechnology Center supported the biotechnology industry.

In examining these theoretical proposals and case studies together, at least two characteristics of industrial clusters can be identified. First, to be an industrial cluster, 'a critical mass' of companies and supporting organizations should be agglomerated spatially, so that in-person interactions can easily happen. Second, social institutions or an entrepreneurial system should be constructed or unfolded to generate and sustain economic dynamism, which nurtures start-ups, promotes knowledge-sharing, supports social learning and facilitates joint-problem solving practice. The local institutions and connections nurture start-ups, and competitive advantages pull established companies to the area. With more entrepreneurial entities and human talent, a region becomes an ecological system with a ‘critical mass’. At the same time, certain types of local practices and understanding – in building up business, in interacting with each other, in communicating, in addressing common issues and so forth – arise and are shared in the community, which lead to the development of social norms and relationships. In sum, the previous studies give a large focus to the competitive advantages of industrial districts, but they shed little light on where start-ups and institutions come from. Therefore, it is still mostly unanswered how a critical mass of organizations emerges and how the unique social structures are constructed in the process.

## 2-2. Role of Research Universities in Formation of Industrial Clusters

### *2-2-1. Research Universities and Regional Economic Development*

Drawing on the previous section of the literature review, the function of research universities in nurturing industrial clusters can be divided into two categories: as an anchor of resources, and as an agent of constructing and shaping social structures. The first role mostly revolves around knowledge transfer, which is translated into local economic activity: academic scientists turn into entrepreneurs to commercialize their research from the laboratory; entrepreneurs prefer to establish start-ups in proximity to universities due to the better accessibility to talent and technologies; established companies often move in to capitalize on the function and facilities of university. On the other hand, a research university and its members could be actively involved in creating and invigorating social hubs for networking, collaborating, mutual learning and community initiatives. Through initiatives and leadership of local universities, the local community can build identity, collaborative norms, and partnership. An alumni organization itself can be a core institution of connecting graduates and coordinating interests.

Related to the extent of university's significance, we need to pay attention to two different perspectives: one is the so-called ‘linear model’, which focuses on the heterogeneity between academia and industry; recently, large scholarly attention is being paid to changing characteristics of research universities, which are referred to as ‘entrepreneurial universities’ or ‘science entrepreneurship’. As these concepts imply, the second perspective emphasizes the convergence of academia and industry, and the more extensive engagement of universities in regional economic development. The former perspective is well embodied in Vannevar Bush's (1999[1945]) report, *Science-The Endless Frontier,* which has been the foundation for the federal government to fund academic research since World War Ⅱ. In the report, Bush argued that if the public sector supports basic research at universities, the private sector will translate the knowledge and discoveries into products and processes. The linear model indicates that research universities and research institutions are devoted to basic research, whereas the industries apply basic concepts in producing goods and services, which comprise economic activity (Rosenberg & Nelson, 1994; Nelson & Romer, 1996; Etzkowitz, 2004). According to this perspective, public support to academic research is essential to stimulating innovation because the basic research sector cannot be conducted by the private sector due to externalities and high-risks. In the modern economy, the creation of, for example, the biotechnology industry is attributable to the breakthrough discoveries and technologies at academic laboratories.

This perspective implies that the connections between academic research and commercial applications, and the interactions between universities and industries are difficult to maintain since these two sectors diverge from each other in their focuses, orientations, values and expertise (Rosenberg & Nelson, 1994). Whereas the commercial sector focuses mostly on product development and process innovation to achieve a relatively short-term payoff, academic researchers are committed to creating and expanding knowledge by discovering fundamental mechanisms and processes. In this line, some studies argue that it is the private industries who have the role and responsibility of stimulating economic vitality through innovation and commercialization (Mansfield, 1991; Cohen, Nelson & Walsh, 2002). According to a survey asking the contribution of academic research to developing products and processes, only one-tenth of new products and processes having entered into the marketplace have their origin in universities (Mansfield, 1991). Cohen, Nelson and Walsh (2002) found that the contribution of public research to innovation is far less than other sources, which include customers' feedback or know-how from practice. At the same time, the impact and role of academic research varies substantially across industries – the impact of public research is most significant to drug and medical devices industries.

A group of researchers have studied the role of research universities in constructing industrial clusters, including the link between Stanford and Silicon Valley. For example, Leslie's (2000) study on the origin of Silicon Valley found it was Stanford which brought in contract funding from the federal government and defense agencies from the East Coast to the West Coast during and after World War II. In addition, liaison programs were pivotal in stimulating entrepreneurial activity and attracting established companies from the East Coast to Santa Clara Valley (Adams, 2005). These research findings go along with the study of research parks by Luger and Goldstein (1991), who argue that the presence of research universities and federal research laboratories, and their affiliations with industries are the most important ingredient for the growth of the science parks around this country. In their survey analysis, they find that most companies in research parks were located there to take advantage of research expertise of nearby or affiliated universities. Therefore, they (p. 183) suggested, "the university itself, rather than the affiliated research park, was the more important engine of economic stimulation." This view on the role of research universities is supported by Castells and Hall (1994, p. 231) in their account that "research-oriented universities are to the informational economy what coal mines were to the industrial economy."

Regarding the function of research universities in building up high-technology industries and industrial clusters, a substantial number of papers recognize that research universities play critical roles as seedbeds of high-technology companies and as initiators of entrepreneurial institutions (Prevezer, 1997; Audretsch, 2001; Cooke, 2001; Zucker & Darby, 1996; 2006; Zucker, Darby & Armstrong, 2002). Prevezer (1997) did an analysis to identify factors associated with the generation of biotechnology companies. According to this study, research institutes and their R&D capabilities have been more influential in attracting new biotechnology firms to each state than established companies. Zucker and Darby's (2006) research also underscores the significant impact of prolific academics on the genesis of high-technology companies in nearby localities. They find that a strong spatial association between the number of 'start scientists' and that of start-ups. Zucker and Darby's previous studies with colleagues (1996; 1998) consistently find the knowledge embodied in star scientists is the main seedbed of biotechnology companies.

A number of case studies on regional biotechnology industries provide considerable evidence suggesting that expertise and talent in basic research are the pivotal stimulator of entrepreneurial activity. Smilor, O'Donnell, Stein and Welborn III (2007) traced down the development of three high-technology centers in the U.S. – Research Triangle Park, Austin and San Diego. In the research, they find that research universities have been the engine of creating the centers through transferring technology, formulating business networks, spinning out start-ups and creating a culture of innovation. Walshok et al. (Walshok, Furtek, Lee & Windham, 2002) emphasize the impact of research institutions involving UCSD and local biomedical non-profit research organizations on accumulating research expertise, generating business networks, and attracting and educating skilled workforce as the foundation of biotechnology and telecommunications clusters in San Diego. Especially, UCSD in partnership with the business community has been critical to building up technology capacity and stimulating commercializing activity. Feldman (2003), and Feldman and Francis (2004) also argue that the genesis and development of the biotechnology industry around the Washington, D.C. area lies mostly in the existence of federal research laboratories and universities, which have supplied a pool of technology entrepreneurs and scientists.

Analyses of the geographic distribution of biotechnology companies have important implications for understanding the linkage of research activity and commercial activity. A body of literature verified that a large part of entrepreneurial activity in the biotechnology field has been concentrated in several regions, where outstanding research universities were located (Prevezer, 1997; Cortright & Mayer, 2002; Feldman, 2003; Zucker & Darby, 2006). Several studies suggest that the gap in the growth of biotechnology industry between the U.S. and other developed countries is the result of the difference in research capacity and academic entrepreneurship (Cooke, 2001; Owen-Smith, Riccaboni, Pammolli & Powell, 2002; Lehrer & Asakawa, 2004). American universities and small biotechnology firms take an active role in creating networks and in commercializing R&D findings, while the role of these two groups in European countries is much more limited (Owen-Smith et al., 2002). Cooke (2001), in a comparative study, attributes the robust activity and high interest of universities and their faculty in commercializing laboratory discoveries to the institutional contexts of the U.S.: the federal government puts more emphasis on the potential of commercialization in distributing research funding, and the superior absorptive capacity of the private sector promotes academia-industry collaboration.

As a substantial number of studies indicate, the research capacity and the leadership of research universities are critical to boosting technology entrepreneurship, but the impacts are contingent on the social contexts under which industries and universities interact. In this regard, the impact or role of public research on the local economic development varies substantially between industries (Mansfield, 1991; Cohen, Nelson & Walsh, 2002), organizations (Di Gregorio & Shane, 2003; DeVol & Bedroussian, 2006), historical periods (Rosenberg & Nelson, 1994; Etzkowitz, 2004), regions, and countries (Owen-Smith et al., 2002; Lehrer & Asakawa, 2004). More importantly, the impact of universities depends on their leaders and members' values and attitude toward commercialization, and the strength of linkage with their local industrial community (Castells & Hall, 1994).

### *2-2-2. Mechanisms and Processes of Knowledge Transfer*

While the previous section is about whether research universities are essential for constructing technology industrial clusters, this section revolves around how they can be involved in the process. I review the literature on the mechanisms and processes of research universities’ involvement in developing industrial clusters. In any case, research universities are oriented to conducting basic research and education, neither to developing marketable products nor to gaining profits. Commercialization and marketing are under the reign of industries, which have expertise, facilities and culture for developing marketable goods and services. In the last few decades, concerns and criticisms have been raised over the breach of boundary between academia and industries: universities do translational research of developing prototype products and even conducting early-stage clinical tests; they brought companies onto campus by establishing science parks and incubators; and academics became more interested in commercializing research discoveries than pursuing basic knowledge based on openness and collaboration. On the other side, industries have endorsed the ethos of academic research by allowing and even promoting their scientists to publish in academic journals and to seek fundamental inquiries. But, basically, the two sectors are grounded on distinct norms, values and practices, and they have different interests and functions. Thus, there should be a nexus translating academic invention into industrial innovation.

Roessner (1993) provides an extensive spectrum of interactions between industry and public research laboratories. According to a survey, universities and industry interact through the following ten venues: contract research, cooperative research, workshops including seminars and briefings, licensing, sponsored research, technical consultation, employee exchange, use of laboratory facilities, lab visits, information dissemination through laboratory publications and other documentation. Among these mechanisms, knowledge at federal research laboratories is transferred mostly through person-to-person interactions taking place by visiting laboratories and having personal communications, for example, at seminars. Colyvas et al.'s (2002) case study on 11 licensed inventions by Columbia University and Stanford University underlines Roessner's (1993) finding in that most information regarding novel inventions is circulated within the scientists' circle of academy and industry. Industries monitor, access and acquire knowledge on academic invention through informal daily communications. Liebeskind, Oliver, Zucker and Brewer (1996) found that scientists working at two biotechnology firms published 60 percent of their scientific papers in conjunction with academic scientists, which indicates the ongoing interactions between academic and industrial scientists. Even after leaving academia to found biotechnology companies, most scientists maintain associations with universities as full-time or part-time faculty members (Audretsch, 2001b).

Zucker and Darby (2006) identified star scientists in high-technology fields including biomedical and IT, and found that 72 percent of highly prolific scientists have linkages with industry through patent licensing, joint research and participation in scientific advisory boards, to name a few. They conclude that “the stars themselves rather than their potentially disembodied discoveries play a key role in the formation or transformation of high-tech industries” (In *Abstract*). Zucker and his colleagues (1996; 1998; 2002) consistently suggest that knowledge created at universities is largely transferred to and utilized by the biotechnology industry by means of face-to-face interactions, social ties and social circles, not through formal and legal channels. They (2002) found, for example, that the biotechnology firms with employees who had coauthored academic papers with star scientists have a higher possibility of success in terms of patent granted and product development. Owen-Smith and Powell (2004) also found empirical data suggesting that in a densely collocated biotechnology center, the Boston area, a large part of knowledge is transmitted through informal channels rather than contractual alliances. More specifically, they observed, diagnostic biotechnology firms in Boston absorb local knowledge mostly through informal mechanisms, such as by employing Harvard graduate students, catching ideas and hearing advice from academic scientists.

The key idea here is biotechnology companies are more likely to locate themselves nearby academic scientists who live and work at research universities or non-profit research institutions to keep more intimate contacts with them, since large part of knowledge is transferred through the social process. In other words, as the extent of transferable knowledge is contingent on the spatial proximity, frequency of personal contacts and strength of social networks, companies prefer to stay close to research universities. In addition, a considerable number of studies suggest another mechanism by which research universities are involved in nurturing local industries: academic scientists take their research discoveries to found start-ups in a neighboring community. As a large part of knowledge in biotechnology is embodied in scientists, spin-offs from academic laboratories can be one of the most effective ways of capitalizing on the commercial potential of basic research. As academic scientists tend to stay in their local community to maintain their relationships with universities and peers, in many cases, they establish a start-up next to their university. Location inertia, put forth by Feldman and Francis (2003), applies also to academic entrepreneurs. They (2003, p. 780) accounted for the location inertia as follows:

> Entrepreneurship is an inherently local phenomenon. … In building their companies, entrepreneurs rely on their local contacts, connections, and knowledge of the business environment. Many individuals have location inertia due to reasons such as family mobility constraints, locational preferences, familiarity of the environment, the relatively higher costs associated with changing residence, or the high cost of establishing a new company in a thickly populated environment where office and housing costs tend to be higher.

Audretsch and Stephan (1999) identified the career trajectories of founders of biotechnology firms that had gone public between 1990 and 1992. According to this analysis, half of the total founders have been affiliated with universities as faculty or graduate students prior to their start-up activity. Feldman and Francis's (2003) study on the evolvement of the biotechnology cluster in Maryland implies that research universities and public research institutions play the role of anchoring and supplying technology entrepreneurs. Entrepreneurs from universities play an essential role in translating laboratory knowledge into commercial applications. In fields where knowledge is more implicit and tacit, the in-person engagements of academic scientists, rather than legal contracts or licensing, are the most critical route for channeling research discoveries to regional industries.

To summarize this section, research universities contribute to the accumulation of a 'critical mass' of biotechnology and high-technology companies through two mechanisms. First, entrepreneurs prefer to locate their companies proximate to universities, which are the powerhouse of talent and technology. Second, academic scientists venture into the entrepreneurial world by establishing start-ups nearby their academic laboratory. In this regard, research universities are called 'economic anchors,' 'hotbeds of high-technology industries' or 'the engine of economic growth', since they create and channel knowledge, and a large part of knowledge is commercially exploited locally. As research knowledge is one of the most vital entrepreneurial resources for technology companies, research universities could be regarded as generators and accelerators of entrepreneurial activity.

### *2-2-3. Social Structures and Academia-Industry Interactions*

Increasingly, the literature recognizes that the extent of contribution by a research university to the regional economic development is dependent on social structures and entrepreneurial infrastructure (Walshok, 1999; Florida & Cohen, 1999; Feldman, 2000b; Audretsch, 2001b; Feldman & Francis, 2004). Research expertise is not automatically turned into innovation or entrepreneurial activity, which account for the regional economic performance, because knowledge transfer involves social interactions and engagements. To reach the market, any invention undergoes a lengthy process of reinvention, redefinition and refinement (Nelson & Romer, 1996). Without intimate communication and interactions, the potential of research knowledge will not be fully appreciated or translated into innovation.

This argument implies that knowledge does not move from laboratory to factory without sufficient interactions and relations. If regions are not capable of absorbing local knowledge, they are unable to transform research ideas into the value-added products. Local knowledge is, therefore, exploited by other regions or it will be hidden under a trail of papers (Florida & Cohen, 1999). The degree to which research knowledge is turned into product development relies on 'regional absorptive capacity' in addition to the organizational capacity of universities and companies. The analysis of biotechnology centers in the U.S. by Cortright and Mayer (2002) shows that biomedical research activity has become spatially more dispersed, whereas the commercial activity, such as the formation of biotechnology firms and venture investments, has concentrated more in several regions during the past decades. For biotechnology companies and entrepreneurs, their geographical location is crucial for gaining supports and stimulus. To research universities, it is local environments and contexts which decide, to a large extent, their impact on local economy. In this respect, technology transfer and academic entrepreneurship are a local phenomenon (Aldrich & Fiol, 1994; Baker & Nelson, 2005).

A number of studies argue that the biotechnology industry of the U.S. has dominated the worldwide landscape largely by virtue of its strong research capacity and academic entrepreneurship (Prevezer, 2001; Audretsch, 2001b; Owen-Smith et al., 2002; Lehrer & Asakawa, 2004). It is generally claimed that the interactions between universities and industries in the U.S. are more robust and productive than any other developed countries. The relationship has been constructed, at least in part, by policies and programs of the federal government. The NIH, as the major funding agency for biomedical research, has given a substantial emphasis to academia-industry collaborations and applicability of basic research in dispensing funding (Owen-Smith et al., 2002). Second, some researchers suggest that the institutions and policies of the federal government, such as the Bayh-Dole Act and the Small Business Innovation Research (SBIR) program, have significantly contributed to facilitating knowledge transfer and promoting academic entrepreneurship (Feldman, 2000b; Feldman & Francis, 2004).

The developed countries have benchmarked the U.S. to nurture their biotechnology industry. Both German and Japanese governments, for example, initiated programs encouraging scientists to establish start-ups by giving more credit to the translational aspect in research proposals in allocating research funding, and by trimming down regulations at universities (Lehrer & Asakawa, 2004). According to Govindan (2005), the Singapore government mandated public research organizations to collaborate with industries, and revamped their science park system in a way to promote interactions along with a dramatic increase in investments in the basic biomedical research.

At the local and regional level, economic development strategies, liaison programs, leadership, social networks, culture and specialized services for business were pointed out as necessary infrastructure for capitalizing on academic knowledge to create jobs and to develop industrial centers. First of all, outreach programs and strategies initiated by universities were given high marks as the right tool for knowledge flow. For example, Leslie (2000) and Adams (2005) attributed the formation of Silicon Valley to the affiliates program of the engineering department at Stanford University. These programs have played a role of connecting academic researchers with entrepreneurs and bringing the culture of industry into academia.

Besides liaison programs, each research institution has regulations and guidelines regarding its members engagements with industries. Each funding agency requires its grantees to be consistent with its guidelines on conflict-of-interest, and each university also examines any possibility of conflict-of-interest and conflict-of-commitment involved in its faculty's relations with industries. Most universities operate technology transfer offices, through which academic members disclose inventions, file patents and arrange legal contracts. Academic scientists should be consistent with these regulations to avoid any institutional and psychological penalty. These regulations at universities aim to balance the needs of commercializing basic research with those of maintaining academic integrity (Matkin, 1990; Etzkowitz, 2004).

The Triple Helix model and the concept of entrepreneurial university were introduced to explain the changes of institutional arrangements related to academia-industry interactions (Etzkowitz & Leydesdorff, 1999; Etzkowitz, Webster, Gebhardt & Terra, 2000). The Triple Helix model indicates that the three sectors – government, industry and academia – have been engaged in an interactive process of creating and recreating institutions to promote knowledge transfer. Etzkowitz's (2004) concept of the 'entrepreneurial university' also has implications for understanding institutional changes at research universities. In his analysis of MIT, Etzkowitz (2004) found that MIT constantly created and renovated its institutional arrangements to be an 'entrepreneurial university' throughout the 20th century. For instance, MIT legally allowed its faculty to give consultation to industries by setting up the 'one-fifth rule' in the early 20th century, and they engaged in creating the venture capital system in the Boston area with the hope of promoting start-up activity. The University of California (UC) has also undertaken a long journey for allowing its members to be involved with industries, but, at the same time, maintaining its boundary as a public university. As one of the experiments, UC raised the inventor's share of royalties to 50 percent from between 25 and 15 percent in 1963 to increase disclosures of invention. Since the late 1980s, each campus began to establish a campus-based technology transfer office to manage licensing and patenting, while keeping a central authority of coordinating (Matkin, 1990).

### 2-3. Economic Activity and Knowledge Transfer as Embedded Practices

In the previous section, I reviewed the literature on industrial clusters and knowledge transfer between academia and industries. As pointed out, the development of industrial clusters is dependent on interactions and collaborations between multiple players; the roles of research universities and the extent of knowledge transfer are attributable to interactions and communication between academia and industries. Also, the literature implies that the interactions and collaborations between multiple players are the product of social structures, to a large degree. However, the previous two sections did not provide theoretical frameworks or concepts for understanding the role of social structures in enabling or constraining individuals' economic activity. In this section, I expand the literature review to explore the nexus of social structures and economic activity by focusing on how social structures influence the process of economic development and knowledge transfer.

The mainstream literature from the discipline of economics assumes that human agents do economic activity only to achieve maximum utilization by fine-tuning economic decisions with price information. In the neoclassical economic models, human actors are assumed to take actions in concert with prices without much consideration of social contexts. In these models, it is taken for granted that knowledge and technological discoveries are non-rivalry and non-excludable goods, so all countries or regions have the same chance of utilizing them. In this sense, the aggregate output of any national economy is the product of the amount of capital invested and labor employed. This view is represented by the simple Cobb-Douglas model: what determines the rate of economic growth is the stock of labor and capital. The incomes per capita across countries tend to converge as time goes by: the low income countries accumulate capital faster than developed countries, because the former's rate of investment return is higher as the capital invested is marginal compared to labor.

But as demonstrated in the literature from various disciplines, people do not strictly conduct economic activity only to maximize their utility function as a rational atomistic actor. Economic activity is, to a large extent, enabled and constrained by the social structures in which individuals live. By the same token, entrepreneurs refer to social structures in embarking on entrepreneurial endeavors. Each activity should be legitimate and feasible with elements of social structures, like social ties, norms, regulations, culture and polity. Entrepreneurs need to rely or capitalize on social institutions in conducting a variety of activities: mobilizing resources through social ties and status, building enterprises aligned with legal frameworks, and running businesses in accordance with social legitimacy. The economic prosperity of nations and regions have not converged, nor seem to converge in the future. Countries and regions have taken heterogeneous trajectories of economic development depending on their cultural and historical contexts. We even observe different ways of doing economic activity between ethnic groups, religious groups, social classes and families.

Granovetter (1985, p. 487) refuted both the neoclassical view and the institutional determinism by arguing: "actors do not behave or decide as atoms outside a social context, nor do they adhere slavishly to a script written for them by the particular intersection of social categories that they happen to occupy." Long-term transactions and contracts are possible only between individuals who trust each other. As trust is mainly derived from social relations, individuals' economic activity is embedded in their social relations. Granovetter regards social structure as a web of personal ties, which is the main tool for building social trust and enabling economic transactions at the community level. In his later study on economic activity and organization of ethnic groups, he (2000) reaffirmed that social practices and logics influence the ways of mobilizing and managing resources.

Uzzi (1997) did an ethnographic study on the apparel industry of New York City. In this fieldwork, he found that accessing valuable resources, sharing tacit knowledge and collaborating with each other to address mutual problems takes place only between entrepreneurs having social relations. The transactions either of resources or information occurring between socially tied parties involve tacit and cultural dimensions: "information exchange in embedded ties is more tactic and holistic in nature than the price and quantity data exchanged in arm's length ties" (Uzzi, 1997, p 46).

In other respects, cognition, culture and the political system should be taken into account along with social relations. In interacting to achieve economic goals, individuals and groups refer not only to social relations but also to cultural, political and regulatory contexts. North (1990) focused on the effects of institutions on the costs of transacting (exchange) and transformation (production). The willingness and the fulfillment of entrepreneurial endeavors to exploit economic opportunities are contingent on the institutional framework. People take actions based on their interpretation of the institutional framework, because incentives and rewards (also penalties) are defined by the social institutions.

How social institutions shape entrepreneurial endeavors is well described by Geertz (1963) in his ethnographic study of two Indonesian towns during the 1950s. Geertz (1963, p. 28) stated that "the problem of economic development presents itself primarily as an organizational one." The entrepreneurs – in this study, they refer to a burgeoning group of manufacturers and traders – did not lack resources or entrepreneurial spirit, but they did not have social and economic institutions on which they could build up enterprises. As Geertz (1963, p. 28) concluded:

> What they lack is the power to mobilize their capital and channel their drive in such a way as to exploit the existing market possibilities. They lack the capacity to form efficient economic institutions; they are entrepreneurs without enterprises.

According to Polanyi, the market economy was itself created and controlled by continuous interventions by governments. Polanyi (2001[1944], p. 145) wrote:

> There was nothing natural about laissez-faire; free markets could never have come into being merely by allowing things to take their course. Just as cotton manufactures – the leading free trade industry – were created by the help of protective tariffs, export bounties, and indirect wage subsidies, laissez-faire itself was enforced by the state.

The market economy of the U.K., which led the industrial revolution, was the product of the transformation of labor, land and money into commodities, which could be exploited or employed for the production and trade of goods and services. As argued by Polanyi (2001[1944]), the three elements – labor, land and money – were not commodities in origin, because labor and land were embodied in human being and nature respectively, and money was a tool for exchange invented by financial institutions. An economic system, in which individuals do economic activity, was constructed by governments or political groups.

If we look at the trajectory of economic activity, it continually changes over time. What makes an economy of a city or region thrive and grow, or stagnate and decline? How is the dynamic process of the economy contingent on social structures? Since neoclassical economists were unable to explain the reality – for example, a growing variance in economic growth rates across countries – some of them have turned their attention to the role of technological advance and knowledge on economic growth. This frustration and new perspective are well represented in Solow’s (1994, p. 48) note: "technological progress is at least partially endogenous to the economy,” therefore, Solow (1994, p. 51) concluded: “I think that the real value of endogenous growth theory will emerge from its attempt to model the endogenous component of technological progress as an integral part of the theory of economic growth." Romer (1994) noted that "economic growth occurs whenever people take resources and rearrange them in ways that are more valuable." It is not physical capital or the amount of labor, but rather the 'recipe' that determines economic development. The rate of generation and adoption of new ideas is determined by institutions, population, market size and human capital, not by physical capital (Jones& Romer, 2009).

Hirschman's (1958) view of economic development sheds light on the role of knowledge and strategies on economic development. As Hirschman (1958) pointed out, the merits of developing new industries and of attracting foreign investments lie in learning new technology and practice. Hirschman (1958, p. 36) explained that individuals and organizations develop entrepreneurial abilities and skills in the process of doing and participating: "the ability to invest is acquired and increased primarily by practice; and the amount of practice depends in fact on the size of the modern sector of the economy." He (1958) drew further attention to the importance of human willingness and capacities to lead economic development efforts by noting:

> Development depends not so much on finding the optimal combinations for given resources and factors of production as on calling forth and enlisting for development purposes, resources and abilities that are hidden, scattered or badly utilized (p. 5)… The fundamental problem of development consists in generating and energizing human action in a certain direction. (p. 25)

Resources for entrepreneurial activity do not make much difference even for developing countries or regions. As Hirschman (1958, p. 25) emphasized, "the fundamental problem of development consists in generating and energizing human action in a certain direction." And the energies and capacities of activating and organizing resources are developed in the process of engaging in economic activity.

Schumpeter (1983[1934]; 1962[1942]) pointed to entrepreneurs and small-sized enterprises as the agent who combines resources in a novel way and leads the economic development efforts through 'creative destruction'. He (1962[1942], p. 83) wrote: "The fundamental impulse that sets and keeps the capitalist engine in motion comes from the new consumers' goods, the new methods of production or transportation, the new markets, the new forms of industrial organization that capitalist enterprise creates." Development itself is a discontinuous and deviating process from the status quo. Entrepreneurs, according to Schumpeter (1962[1942], p. 132), are the agents who initiate and implement the creative destruction:

> The function of entrepreneurs is to reform or revolutionize the pattern of production by exploiting an invention or, more generally, an untried technological possibility for producing a new commodity or producing an old one in a new way, by opening up a new source of supply of materials or a new outlet for products, by reorganizing an industry and so on.

If an economy is dominated by handful of bureaucratized giant corporations, entrepreneurs and small or medium-sized firms become marginalized, unable to find resources. Thus, any monopolized economy inevitably loses its economic dynamism, and finally heads to a decline.

Jacobs (1970; 1985) is also in the line with Schumpeter's point of view, which attributes economic development to the destructive process of reorganizing ongoing processes and mechanisms. Jacobs argued that economic development of cities is determined by their capability of improvising new products and services, and applying them into economic activity. Cities, which continue to provide the learning opportunities and resources necessary to turn learned skills and insights into products and services, can enrich and ramify their economic activity. Capacities of improvising, improving and innovating are the consequence of experience and engagement, as Jacobs noted (1970, p. 55): "the point is that new goods and services, whether criminal or benign, do not come out of thin air. New work arises upon existing work; it requires 'parent' work." She (1970) compared the divergent fates of two English cities, Manchester and Birmingham. By the 1840s, Manchester was the most advanced city in terms of industrial development because of its textile industry and its large corporations. However, its monopolized industrial structure and abominable living condition for ordinary people virtually prohibited small enterprises from spawning out. In Birmingham, in contrast, a mass of small and medium-sized companies composed the industrial landscape of the city. As time had passed, “Manchester’s efficient specialization portended stagnation and a profoundly obsolescent city…The economy of Birmingham did not become obsolete, like Manchester’s. Its fragmented and inefficient little industries kept adding new work, and splitting off new organizations, some of which have become very large but are still outweighed in total employment and production by the many small ones” (1970, p. 88-89).

She claimed that "development is a do-it-yourself process; for any economy it is either do it yourself or don't develop" (1985, p. 140). Only at a diversified and versatile economic setting, employees could continuously develop and upgrade their skills and motivation for starting businesses. A diversified economy allows employees to be involved in a variety of activity from which they gain knowledge and develop practices. As she noted, "invention, practical problem solving, improvisation and innovation are all part and parcel of one another" (1985, p. 150). If employees can access financial resources and the necessary business services, many of them venture into the entrepreneurial world. This is the process of multiplication and ramification of economic activity – and, in the long-term, economic development.

Sabel (1982) was intrigued by the rapid expansion of small shops and factories in the Third Italy during the period of the 1950s to 1970s. Sabel attributed the generation and ramification of the small firm economy in the Third Italy to their technical versatility and frequent interactions with related firms in the community:

> The innovative capacity of this type of firm depends on its flexible use of technology; its close relations with other, similarly innovative firms in the same and adjacent sectors; and above all on the close collaboration of workers with different kinds of expertise. (1982, p. 223)

Founders and employees of these specialized small enterprises are constantly required to deal with ongoing problems – producing and marketing products, addressing consumers' complaints, surviving competitions and so on – by innovating products and processes. In this process, the workers gain knowledge and develop practices. When feeling confident with their ability and finding new opportunities, they embark on new enterprises.

In this line, Piore and Sabel (1984) ascribed the crisis of world economy during the 1970s to the rigid mass production system built on mass investments in physical facilities, exploitive relationships with employees and subcontractors, and bureaucratic welfare governments. Under this system, large companies are reluctant to adopting new technologies, small companies have little ability to innovate, and organizations avoid sharing knowledge. As alternatives, they suggested a flexible and interdependent system under which individuals, as entrepreneurs or employees, are more independent and autonomous, so they could cooperate and develop skills. This idea was built on their studies of specialized industrial districts, where each sector of economy and society is seamlessly linked to each other. In the industrial districts, economic and political constituents collaborate to train employees, attract financial resources and share knowledge through close-knit social ties. Consistent with these claims, Norton (2001) found that the revival of the U.S. economy during the 1990s was rooted in the new logics and practice of the West and South region. Since the 1990s, the U.S. has become the fastest growing economy among the developed countries, and has regained its prominence over the world economy. The transformation was brought by newcomer firms in the Sun Belt and the Pacific Coast, which had developed and adopted a new paradigm based on networking, collaborating, experimenting and taking risks.

Economic dynamics and vitality of regional economies depend on their capacity and willingness to invent and innovate in the long-term. Through diversifying and improving their products and services, a society continues to create job opportunities and increase incomes of ordinary people. Innovation begins by discovering tacit dimension in knowledge, which is not yet tapped in on-going technologies, markets or organizations. The discovery of a hidden dimension in knowledge is the consequence of interactions and communication in a network of people, where multiple ideas and perspectives congregate (Ogle, 2007). Innovation and creativity involve long-term efforts and engagements both with people and problems, not the result of a Eureka moment (Ogle, 2007; Johnson, 2010). Social relations and trust enable individuals to interact with each other by activating person-to-person communication and preventing opportunism. To discover novel concepts and to translate new ideas into economic activity, entrepreneurs have to live in an environment, where institutions and culture promote entrepreneurship. As Hirschman (1958) emphasized, norms, practice and human relations in a community are the essential element of constructing and mobilizing resources. Then, how do practices and social institutions stimulating innovation and entrepreneurial activity emerge and evolve?

The study on social capital by Putnam (1993) has an important implication to this question. In an analysis on the differences in economic prosperity between Italian regions, particularly between the Southern and Northern regions, Putnam (1993) concluded that each region's economic performance depends upon its stock of 'social capital'. Civic engagement, termed 'social capital', enables small firms to cooperate to share knowledge, resources and social services at the same time to compete. Collaborations are routinely carried out only in the regions where citizens embody norms of reciprocity, mutual trust and civic engagement. As Putnam (1993) observed, small firms in the Third Italy are collaborating while competing through cooperative horizontal networks. Small firms become specialized and flexible, because they can employ services and technologies from outside, and also they can partner with trade associations for services in common. The high social mobility and information flows within this district enable small firms to be on the edge of innovation. Generalized reciprocity and trust within a community have been developed in the process of repeated social interactions. People learn how to cooperate to promote mutual benefit through civic engagements, and the experiences are embedded in their norms and culture incrementally, which lead to the creation of social capital.

Putnam looked back to the medieval age of the 12th century to trace the origins of divergence in social capital between the Northern and Southern Italy. While the Southern regions were controlled by autocratic rules, the people in Northern part of Italy lived under a communal republic system, where civilians founded autonomous associations and did economic activity based on mutual covenants and contracts. Under autocratic regimes, the Southern regions did not experience any horizontal cooperation and civic engagements. In authoritarian society and under patron-clientelism relationship, any horizontal cooperation is constrained because people do not govern themselves – they are controlled by political elites. Thus, people cannot practice civil engagements under such a socioeconomic environment. This historical legacy, Putman concluded, decided the economic prosperity: the northern part of Italy thrives as the most innovative economy, but its southern regions suffer from economic stagnation.

The literature highlights the role and impact of social structures on economic development. In short, economic activity and innovation are embedded in social structures. Human beings as economic agents are enabled and constrained in embarking on entrepreneurial and innovative endeavors by their social structures. Piecing together the claims of Schumpeter, Jacobs, Hirschman, Romer and Sabel, the rate of economic growth is determined by the capacity and conditions for stimulating innovation and creating knowledge. Putman's study suggests that mutual engagements and interactions shape social structures.

### 2-4. Social Structures, Practices and Learning

The literature consistently found that entrepreneurial activity and interactions, in various forms, are dynamic and robust in industrial clusters. In industrial clusters, more start-up activities and interactions between constituents take place. The literature on the roles of research universities and technology transfer suggests that transfer and translation of research discoveries take place through social processes and mechanisms. In the previous section, I reviewed the literature on the embeddedness of economic activity (and economic development as a dynamic trajectory of economic activity) in social structures. However, the literature on industrial clusters, technology transfer and social embeddedness offers little insight into the constitutive process or the social structures underlying entrepreneurship and interactions. Therefore, this section of the literature review revolves around questions of how social structures define patterns of individuals' actions and how social structures are constructed by individuals' practices. To say again, I focus on the mutually constitutive relation between social structures and human beings' practices: how social structures influence individuals' practices either as an enabler or constraint; and how individuals' practices enact or develop social structures. To answer these questions, I start with Giddens's theory of structuration and look into the literature on theories of social structures. Then, I look into how individuals embody social structures and develop their identities and knowledge through situating them in social structures or communities of practice. For this, I draw on a set of organizational theories ranging from Weick's sensemaking to Wenger's communities of practice.

Giddens's (1979; 1984) theory of structuration draws attention to recursive practices of everyday life, and argues that contexts and conditions lead to 'continuity of practices'. Human agents take actions drawing on the 'stocks of knowledge', which were constituted under their time-space context. As Giddens noted, "actors employ typified schemes (formulae) in the course of their daily activities to negotiate routinely the situations of social life” (1984, p. 22). In this view, social practices are situated in social structures, which Giddens defined as "rules and resources, recursively implicated in the reproduction of social systems" (1984, p. 377). In this sense, rules (or interpretive schemas) and resources do not exist on their own; they are enacted by practices of human agents. They are embodied only through repetitive practices, and have different meanings depending on how they are enacted. Social systems are produced or reproduced only through the continuity of social practices. Therefore, social structure and practices taken by human agents are mutually constitutive. All social practices are situated in social structures, and by the same token, social structures are constituted by practices of individuals.

Sewell (1992) argues that how rules and resources constitute or reconstitute social structures remains unspecified in the theory of structuration. Sewell redefined social structures as "sets of mutually sustaining schemas and resources that empower and constrain social action and that tend to be reproduced by that social action” (p. 19), and agency as "the capacity to transpose and extend schemas to new contexts" (p. 18), which is "formed by a specific range of cultural schemas and resources available in a person's particular social milieu" (p. 20). A duality exists between schemas and resources in that the enactment of resources depends on schemas on which human agents draw in taking actions. In Sewell's words (p. 19), "any array of resources is capable of being interpreted in varying ways and, therefore, of empowering different actors and teaching different schemas." On the contrary, resources have "a crucial weight in shaping and constraining social life in particular times and places" (p. 9). Resources consist of human resources such as strategy, tactics, regions, and non-human resources such as factories, armaments and land.

Increasingly, the literature recognizes that resources are enacted by practices and schemas of human agents. Orlikowski (1992; 2000) looked at the structurational process of a newly introduced technology. She found that the practice of a technology is socially constructed in the process of interpreting and appropriating it by users. According to this perspective, the meaning and impact of technology are constructed in accordance to users' enactment in their everyday life. At the same time, technologies in social life become part of structural properties, which frame human activity: Orlikowski (1992, p. 406) explained this aspect of technologies: "it is also the case that once developed and deployed, technology tends to become reified and institutionalized, losing its connection with the human agents that constructed it or gave it meaning, and it appears to be part of the objective, structural properties of the organization.” Resources are not static or exogenous assets, but they are constantly created and reproduced by practices or organizational routines (Feldman, 2004). In the words of Feldman (2004, p. 296), "resourcing is the creation in practice of assets such as people, time, money, knowledge, or skill." In this line, Feldman and Quick (2009) suggested that resources in area of public policy, which include mutual trust, public participation and legitimacy, be generated and redefined by actions of constituents. Once resources are enacted through a sequence of interactions and inclusions, they generate frameworks that channel future public actions into a certain pathway.

As the duality of social structures and human actions tells, individuals are involved in the process of constructing social structures as they exercise interpretation and take action in social settings. At the same time, social structures that are enacted by human agents' practices become references for future actions and interactions as forms of norms, principles, protocols, guidelines and ethics. Then, the next question is, how do individuals enact and embody social structures in their everyday life? Regarding this question, Weick’s (2001) concept of sensemaking provides a valuable guide in linking people's interactions and the formation of social structures. According to her, the formation of social structures is the product of people's interpretations of social interactions. Social structures emerge in the course of seeking to justify interactions. Individual's micro interactions that take place in each social setting translate into macro institutions. Weick (2001, p. 26) wrote:

> Thus, social order is created continuously as people make commitments and develop valid, socially acceptable justifications for these commitments. Phrased in this way, individual sensemaking has the potential to be transformed into social structures and to maintain these structures.

Cohen and Bacdayan's (1994) experiment is worth noting, in that they give another perspective on how routines arise and become embodied in the process of learning and acting on procedural rules. Drawing on an experiment, they found that the root of organizational routines lies in individuals' learned and stored skills and memories, which are repeatedly referred to in taking further actions. Individuals refer to their 'procedural memories' in taking actions at an organizational setting. As Cohen and Bacdayan (1994, p. 557) noted:

> As individuals become skilled in their portions of a routine the actions become stored as procedural memories and can later be triggered as substantial chunks of

> behaviors. The routine of a group can be viewed as the concatenation of such procedurally stored actions, each primed by and priming the actions of others.

Like Weick's sensemaking, Cohen and Bacdayan's view of organizational routine pursues to link the construction of social structures with individuals' practice.

The inquiry on the emergence and production of social structures is crucial to explaining the dialectic relation between social orders and practice of human agents, in other respects, we need to pay attention to how individuals are engaged in embodying, enacting and reproducing interpretive schemas and resources in a situated way. Any social group or organization constructs and reproduces a set of routines, whereby their constituents find meanings, take actions, and produce artifacts. It is important to see what takes place in each social community: how individual members take 'situated actions and interpretations', how individuals' 'situated practices' construct or reproduce interpretive schemas of their community, how individuals embody organizational routines, and how newcomers become members of community.

The literature on social learning and communities of practice – I will use the term *communities of practice*, following Wenger, McDermott and Snyder (2002, p. 4) to refer to “groups of people who share a concern, a set of problems, or a passion about a topic, and who deepen their knowledge and expertise in this area by interacting on an ongoing basis" – is essential in theoretically understanding the dynamic process of structuration. A body of literature claims that the formation of a web of local meanings is rooted in the learning and negotiating process through interactions. Learning and knowing are the process of situating oneself in the collective of local meanings. By participating in the practices of communities, individuals appreciate and embody the web of the local meanings. The way individuals know and learn the local knowledge is to experience and engage in constructing and reconstructing the meanings (Lave & Wenger, 1991; Orr, 1996; Wenger, 1998; Yanow, 2003).

Learning happens through involvement in negotiating practices of a community (Lave & Wenger, 1991). Through participation in communities of practice, newcomers absorb the practice which constitutes the community. In this sense, according to Lave and Wenger (1991, p. 31), "learning is an integral and inseparable aspect of social practice." To learn and embody social practice, newcomers should be able to participate legitimately in communities of practice, and to situate themselves in the ongoing constitutive process. Local meanings are constantly produced and reproduced in the process of members' interactions (Wenger, 1998). In this respect, individuals learn by taking part in creating and shaping local meanings and practices of communities. Learning occurs in the process of experiencing and interpreting the world and the relations of self with the world as a participant of a community. Therefore, in words of Wenger (1998, p. 96), "such learning has to do with the development of our practices and our ability to negotiate meaning. It is not just the acquisition of memories, habits, and skills, but the formation of an identity."

To perceive and absorb the experiences through interactions, individuals need to understand the meanings and values of organizational artifacts, which include language, symbols, stories, and norms. Again, to be able to interpret organizational artifacts, individuals need to have participated or participate in organizational practices, whereby meanings and values of organizational artifacts are defined and reproduced. To be competent, individuals of a community should be able to take actions and make decisions in accord with the practice of their community. The interpretations and actions should be legitimate and valuable from the eyes of their belonging community. Observational research, done by Orr (1996), Orlikowski (2002) and Strati (2003) provides an in-depth insight into how individuals learn and enact organizational routines through everyday practice.

Orr (1996), in an ethnographic study on a community of photocopier technicians, observed that the technicians learn skills by constructing narratives and conversing with their colleagues. By practicing and participating in making stories in communities, the technicians construct their identity as well as develop their profession. Orr (1996, p. 2) noted:

> Narrative forms a primary element of this practice. The actual process of diagnosis involves the creation of a coherent account of the troubled state of the machine from available pieces of unintegrated information, and in this respect, diagnosis happens through a narrative process... The circulation of stories among the community of technicians is the principal means by which the technicians stay informed of the developing subtleties of machine behavior in the field. The telling of these narratives demonstrates and shares the technicians' mastery and so both celebrates and creates the technicians' identities as masters of the black arts of dealing with machines and of the only somewhat less difficult arts of dealing with customers.

To learn from narratives, members need to have shared experiences in common, on which stories are constructed. Without the shared experience, the participants have difficulty in understanding narratives. So, the problem-solving in the field requires that practitioners exercise 'situated interpretation' and construct narratives that represent their reflections of social situations. Instructions in written form have, indeed, limited capability of transferring knowledge, since a large part of information necessary to interpret each contextual situation is omitted under a premise that such information is already shared among practitioners. The entire knowledge of diagnosing and fixing machines, Orr contended (1996), cannot be, practically, inscribed in documents.

Orlikowski (2002) looked at how a multinational company coordinates with local development units located across 15 regions. In this field research, Orlikowski found that knowledge is constructed by and present in the practice of constituents, and the competence of an organization is contingent upon the routines of their employees. As she argued (2002, p. 269), “through engaging in these practices, members of a company are able to knowledgeably navigate and negotiate the multiple boundaries that they routinely encounter in their daily work-boundaries of time, space, culture, technology, history, and politics.” Strati (2003) claimed that individuals learn through participating in practices of organizations. Strati (p. 72) referred to what individuals learn through interactive processes as 'aesthetic knowledge': "aesthetics, in fact, closely interweaves with the tacit knowledge of individuals, and they both signal the socially constructed personal way in which people interact to invent, negotiate, and recreate organizational life through practice, taste, and learning."

Brown and Duguid (1991) applied the learning process in communities of practice to the understanding of studies explaining innovation and creativity. According to them, innovation arises in communities of practice, where members engage in narrative activity and interact with each other to solve problems. Working, learning and innovating, as noted by Brown and Duguid (1991), take place simultaneously as individuals engage in practices of their communities. In the process of diagnosing problems and inventing solutions by creating and reshaping narratives, participants come across and absorb novel concepts and perspectives. Since a large part of knowledge is embedded in collective experience, narratives and artifacts of communities, individuals access and recognize the hidden dimension of knowledge by participating in practices in common. In their later research (2000b, p. 18), they wrote that "for all information's independence and extent, it is people, in their communities, organizations, and institutions, who ultimately decide what it means and why it matters." In the end, human creativity comes not from information, but from knowledge that can only be gained through interactions and involvement in communities of practice.

Tacitness in knowing and learning, as suggested by Polanyi (1966), has an important implication to understanding why knowing involves doing and interacting. Furthermore, the nature of knowledge indicates the intrinsic limits in translating and transferring meanings and experiences by formalized artifacts. Through reification, people seek to sophisticate, share and store their interpretations of the social world, but, as Polanyi claimed, a large part of meanings should involve 'common sense' to be shared. Polanyi (1966, p. 4) pointed out that “we can know more than we can tell” since some part of knowledge cannot be fully described and transferred in a codified form. Codified or explicit knowledge refers to knowledge that can be articulated and communicated in a formal code, whereas tacit knowledge requires face-to-face contact, personal relations based on mutual trust and shared experience to be transferred. In other words, knowledge should involve personal interactions and shared experience to be circulated in addition to documents or written manuals.

One of the channels for acquiring tacit knowledge is apprenticeship, through which students learn from their mentors by observing, imitating, and practicing (Nonaka, 1994). The boundary between tacit and explicit dimensions is not clearly distinguishable or permanently fixed (Nonaka & Takeuchi, 1995). Nonaka (1994) argued that the tacit part of knowledge can be converted into more explicit and transferrable forms through “the successive rounds of meaning dialogue” (p. 20) between team members. Team members can convert the tacit dimension into a codified one – termed as ‘socialization’ by Nonaka – by articulating and adding their own experiences and perspectives based on interaction and communication. Nonaka and Takeuchi (1995) claimed that Japanese companies have been successful thanks to their capacity of learning and translating the tacit part of knowledge. These studies imply that the tacit dimension in knowledge can be acquired, shared and accumulated within communities of practice, where members have constant interactions to solve ongoing problems.

Therefore, a stock of knowledge is constructed, reproduced and interpreted, to large extent, within the boundary of communities of practice. To learn and enact local cultural schemas, individuals should locate themselves in ongoing situations by participating in actions and interactions of everyday life. The learning and reification process suggests that a group of people having a set of issues and initiatives in common creates and reshapes the significance and signification of mutual experience through interactions. It is a local community of practitioners, in this sense, who develops knowledge and practices to address their problems. Therefore, newcomers learn knowledge and practices by participating in the problem-solving process in communities of practice.

In sum, on the one hand, social structures enable and constrain human practices, but, on the other hand, human practices shape social structures in the process of learning and interacting. Communities of practice are the space where individuals embody and enact social structures by participating in the interactions and routines. The main suggestions of the literature include:

- Human agents take actions situated in social structures, which consist of interpretive schemas and resources.
- Structural properties, including schemas and resources, are constructed through individuals' practices and routines. In other words, interpretive schemas and resources are enacted by people's practices.
- By engaging in social actions and interactions, individuals access and acquire knowledge and practices of communities.
- Learning and knowing take place through participating in the activity of communities. And learning is not just absorbing and applying knowledge, but it is becoming.
- Knowledge is produced, stored, transformed and transferred through narratives and artifacts. Artifacts take multiple forms such as stories, repertoires, discourses and symbols, and they represent meanings and interpretations of experience, of both individuals and the group.
- To learn practices of a community, individuals should share common experience and be familiar with meanings of artifacts through participation and interactions.

- As a large part of knowledge is of a tacit dimension, individuals should be involved in in-person interactions and have hands-on experience to learn. In this respect, a large part of knowledge is created, circulated and stored in communities, where members have shared experiences through ongoing interactions and communications.

In the following chapters, I will show how this literature relates to the case of San Diego biotechnology community. As a preview, through my field research I have found the San Diego biotechnology cluster needs to be understood as a community, not as a mechanical collection of resources and actors. The interviews, field observations and archival data consistently indicate that the people working and living in the community share understanding and practices. Many historical episodes show that a set of concepts and practices have been discovered, unfolded and embedded in the community. There exist a variety of organizations and mechanisms which channel social interactions of the community members. As put together, the literature provides theoretical concepts to explain the genesis and development of San Diego biotechnology community's social structures.

# CHAPTER 3: RESEARCH METHODOLOGY

## 3-1. Overview on Research Approach: Interpretive Study

In this study, I focus on discovering the contextual properties and structural elements that underpin the entrepreneurial dynamism of a biotechnology cluster and the constructive trajectory of a community. As pointed out previously, the San Diego biotechnology cluster consists of a set of groups: entrepreneurs, investors, service providers, trade associations, governments, and research institutions. Entrepreneurial activity requires the coordinated efforts of mobilizing resources and organizing expertise across professions. Each specialty group stands on a distinct set of capacity, practice and norms (refer to Chapter 5). Innovation and commercialization, as claimed in the literature, are social and organizing processes. So, we need to pay attention to the underlying structural elements which enable or constrain entrepreneurial activity. At the same time, focus needs to also be given to the developing process of each sector's capacity, practice and norms. Practice and structural properties – interpretive schemes and resources – are constitutive. And the constructive process involves a span of time, during which individuals accumulate their interpretations, and produce artifacts reifying the local web of meanings.

The case of the San Diego biotechnology cluster consists of hundreds of biotechnology companies, several nationally renowned research institutions, dozens of venture and angel investment organizations, groups of specialized service providers, trade associations and collaborative initiatives. More interestingly, this community emerged from scratch to be one of the most dynamic life sciences centers during the last few decades. Biomedical research institutions came for the first time in the early 1960s, and the business community began to appear on the map after 1980s. In these respects, this setting provides an interesting case seeking the following inquiries.

1. *Which elements or properties have enabled or enable the entrepreneurial dynamism to unleash?*
2. *How have these elements or properties been produced or reproduced?*

Among the participating groups, research institutions are noticeably heterogeneous from the business community. The research institutions – both research universities and non-profit research institutes – depend mostly on funding from the federal government, state governments and philanthropists in conducting research projects, and their main interest is to understand the principles of biological mechanisms and processes (refer to Chapter 6). Due to this funding mechanism, the academic scientists work under a distinct context of regulations, recognitions and rewards systems from those in industry. The relationship between organizations specialized in basic research and commercializing activity provides a window into the structural elements that either enable or constrain knowledge transfer. In this regard, the following two questions also will be followed in this research:

1. *Which elements or properties facilitate or limit involvement of academics in entrepreneurial activity and relations with industry?*
2. *How have these elements or properties, which forge patterns of interactions between research institutions and industry, been enacted?*

A large body of literature defines industrial clusters as 'an industrial system', ‘a milieux of innovation,’ 'an ecosystem,' or 'a habitat', where participants construct a unique set of practices and norms through interactions (Saxenian, 1994; Castells & Hall, 1994; Lee et al., 2000). The following is a brief review of the literature, which explains why I drew on an interpretivist approach to answer the research questions. Practices and rules of a community serve as a context to which its members refer to in taking actions. The role and impact of research universities depend on the relationship with their local business community and the degree of its members' entrepreneurship. A large part of knowledge is commercially capitalized through social and relational channels, which often involve personal interactions and mutual engagements. In turning basic research into products, academic scientists have to deal with a set of regulations and peer-pressure. Therefore, we need to see the interpretations and interactions involved in knowledge transfer as social processes.

Drawing on the perspective of social constructivists, social structures of industrial clusters are to be enacted by practices and interactions (Giddens 1979; 1984). As Giddens (1979, p. 54) noted, "all social practices are situated activities" meaning human activity is embedded in social structures. In Giddens’s (1979, p. 66) words, "to study the structuration of a social system is to study the ways in which that system, via the application of generative rules and resources, and in the context of unintended outcomes, is produced and reproduced in interaction." A theory of practice by Bourdieu (Bourdieu & Wacquant, 1992) also suggests that social structures or orders are constructed by everyday's practice. In this line, organizations, noted by Weick (2001, p. 5), are "collections of people trying to make sense of what is happening around them." In the process of negotiating the meaning of experience, communities of practice emerge and evolve (Wenger, 1998). Technologies and resources, which are assumed to be given and fixed in most positivistic studies, are enacted and reproduced by individuals' practices and routines (Orlikowski, 1992; 2000; Feldman, 2004). Reciprocally, once resources and rules are constructed through the enactment of practices in everyday life, they direct the way of acting and interacting to be consistent with the structural elements.

Entrepreneurial activity, such as establishing start-ups, attracting talent and capital, forming partnerships and conducting various activities to commercialize, is embedded in social, cultural and historical contexts (Geertz, 1963; Coleman, J., 1984; Granovetter, 1985). Economic actors take certain patterns of actions and interpretations of experience situated in their social structures. That is, in Bourdieu's words, "the economic behavior socially recognized as rational is the product of certain economic and social conditions" (2005, p. 84). I wanted to understand and explain the structural elements that have nurtured robust entrepreneurial activity and interactions between academia and industry. As the individuals construct social structures by composing interpretations, I aimed to make sense of this community by creating theoretical concepts.

Learning and knowing are the process of situating oneself in the collective of local meanings. By situating oneself within practices of a community, individuals make sense of the web of the local meanings, and enact concepts, largely, in a form of narratives to make sense of the complexity of social order. To repeat, the way individuals know, learn and embody local knowledge is to experience and engage in creating and producing the web of local meanings (Lave & Wenger, 1991; Orr, 1996; Wenger, 1998; Yanow, 2000; 2003; 2006). Thus, I focused on people's experience, and their accounts of experience represented in narratives and communal artifacts. I drew on the interpretive approach and developed my understanding of this methodology because of my stance and interpretation of the nature of society – ontology – and the method of knowing social world – epistemology. I wanted to capture the complexity and dynamism of a community as richly as possible, since the ultimate goal of this research is to understand the invisible, but operative, "webs of significance" (Geertz, 1973, p. 5), to which people situate their actions and create artifacts to reify their interpretations of social interactions.

Instead of looking at 'population' or multiple cases, I chose one locality –San Diego – and one sector (the biotechnology industry), not only to explore the constructive and operative process of an industrial district, but also to shed light on the rise of entrepreneurial centers around the globe. In conducting this research, I have been interested in understanding industrial districts, including Silicon Valley and the Route 128 area, and the national and historical contexts of university-industry relations. In this respect, this is a case study that mainly seeks to construct a conceptual framework to explain the rise of industrial districts, and the construction of academia-industry relationships through exploring the complexity and dynamics of a single phenomenon (Eisenhardt, 1989; Yin, 2003).

### 3-2. Collecting and Analyzing Data

By drawing on the frames of interpretative approach, I sought to discover, identify and explain the experiences and practices of the San Diego biotechnology community as an organization: how people of the local community interpret the meanings of social events, embody their experiences, and enact their interpretations into social structures. The experiences and practices of individuals represent social contexts, as Corbin and Straus noted (2008, p. 10), because "each person experiences and gives meaning to events in light of his or her own biography or experiences, according to gender, time and place, cultural, political, religious, and professional backgrounds."

I employed 'grounded theory' as a primary methodology in accessing, analyzing data and in composing theoretical frameworks. Grounded theory seeks to generate categories and properties of categories by an iterative process of gathering data and conceptualizing them in terms of patterns and trends (Glaser & Strauss, 1967; Corbin & Strauss 2008). Concepts enable researchers to construct interpretive schemes that help understand the complexity of social events. Grounded theory emphasizes iterations between data collection, analysis and conceptualization in discovering, interpreting and theorizing data. The iterative process involves continuous comparisons of theories and data, those of data from different sources, and moving back and forth between research stages (Eisenhardt, 1989). After all, internal validity is reachable only when the findings are firmly and rigorously grounded on the empirical data.

Throughout this research, a large part of data collection, analysis and writing was conducted iteratively. Soon after the end of each interview, I coded and wrote memos after completing transcription. The analysis process often redirected foci of interest, which resulted in revising interview questions, choosing future interviewees and realigning efforts of collecting archival data (Yanow, 2006; Corbin & Strauss, 2008). New concepts and feelings that appeared during interview meetings or field observations were written as memos or they were developed into diagrams. Along with collecting archival data, I chronicled events and accounts into each category, and added analytical memos for the emerging ideas or concepts. On the one hand, the theories have guided the data collection and analysis process, and, on the other hand, the data rejuvenated my interest in the literature, and challenged the theoretical explanations in the literature. I kept reading the literature on methodologies and related fields to articulate, compare and validate evolving concepts and frameworks, which have emerged from the process of data collection and analysis.

I was "there" (in the San Diego biotechnology community) physically for the first time in February, 2008, at a forum – *Creating companies from emerging technologies: Perspectives from Cambridge, Menlo Park, and San Diego* – where I listened to discussions by a group of seasoned entrepreneurs, and was impressed by the "energy" of this networking event. It was a later event in June of 2008, *Connect with CONNECT*, where I started to converse with the local people and to make interview appointments. In 2010, I attended the same event, *Connect with CONNECT*, at the same place, where I could see several exhibitors of 2008 with more sophisticated products and new faces. I did the first interview in July, 2008, and continued through November, 2010. Even before 'being there', I had started to watch and listen to podcasts on UCSD TV, KPBS (a local PBS station) and many other media. The searching and reading of local news media began the 2008 summer, and since then, it took significant a part of my time for the following two and half years.

In the initial stage, I started collecting data that seemed to be related to the research questions. The sequence of events and newspaper accounts of individuals on the events were categorized into several concepts: collaborative culture, leadership, local identity, geographical context, strategies of corporations and spin-off process. The coding and memoing, along with data collection, rendered sophistication and revision of concepts, which reoriented my attention to different types of data, and to a literature body, which gives more relevant theoretical frameworks. Therefore, I drew on 'theoretical sampling', which puts focus on collecting data "from places, people, and events that will maximize opportunities to develop concepts in terms of their properties and dimensions, uncover variations, and identify relationships between concepts" (Corbin & Strauss, 2008, p. 143). In the process, new concepts like 'learning by acting and by interacting', 'forming relationships and identity', and 'practices of entrepreneurship' began to appear. I started recognizing the variation in practices and norms between sub-groups, and between historical periods. At the same time, I also acknowledged the common ground of sub-groups and time periods, which combine as one social setting.

The San Diego biotechnology community is more complex and dynamic than I could fully capture using my own capability and resources. The community consists of hundreds of companies and institutions, and thousands of people, who have unique attitudes, experiences and perspectives to interpret their actions. I was aware that it would be impossible to listen to all the people and trace down all events. Further, I do not believe that one theory or a theoretical framework from one disciple could be the angle or lens through which we can understand the complexity of social reality. A note by Corbin and Strauss (2008, p. 16) has been the compass by which I oriented my research many times: “what is required, above all, is an intuitive sense of what is going on in the data; trust in the self and the research process; and the ability to remain creative, flexible, and true to the data all at the same time.”

The three main sources of data – archival, interviews and field observations – were accessed and exploited all at the same time. Collecting and analyzing data from the local news media proceeded while interviews and field observations were conducted. While transcribing and analyzing interviews, I searched any archival data that was indicated by interviewees, or that would provide further understanding on content. Field observations produced short but vivid conversations with participants, and often the conversing led to interview meetings. Data collection and memoing from one source enabled and enriched the collection and interpretation of other data sources. Research on archival data helped identify interview candidates, and their social backgrounds. In some cases, I met former interviewees again at local events, and some of them introduced me to their colleagues at the spot. Thus, separating sections between collection and analysis, and between sources of data is not in line with the actual sequence or the logic of this research, but it is to organize my experience and theoretical rationale.

### ***3-2-1. Archival Data***

I expected that a major difficulty in collecting data would result due to the confidentiality and privacy of biotechnology firms and employees. Most start-ups have no visible facilities or products, but they have technologies and strategies on which they capitalize to be profitable. The companies without any products or sizable facilities need to protect their intellectual assets. They depend on the system of intellectual property rights to keep the value of companies safe from any 'stealing' by competitors. Therefore, legal disputes between competing companies frequently occur, and in many cases, biotechnology start-ups can be ruined by tedious legal processes. When I started working on this research, and presented the dissertation proposal to the committee, one of their main concerns was about how far I could access the people and artifacts of the local biotechnology community. Moreover, I was a non-native speaker, without any experience in and relations with the local biotechnology industry.

In order to overcome these difficulties, first, I had to know about the community and build relationships. From the beginning, I sought to identify and access potential interviewees and archival data sources. Although the literature and policy analysis reports on the San Diego biotechnology industry provided a lens through which to view the overall landscape, it gave limited information on 'who's who. Not knowing the names of significant players, places and events, it seemed to be impossible to access the right people, and to raise the right questions. In an effort to access the local community, I discovered one venue after another to reach the stock of archives and the network of the community.

During the early phase, I drew on two most important local newspapers: San Diego Tribune and San Diego Union. The newspapers were fully accessible since 1983 via internet, and I looked at every title of articles in the business and opinion sections by opening every daily edition. This work was a time and energy consuming labor, but it produced an unexpected amount of data. A majority of articles were concerned with the activity of biotechnology companies – stories about starting companies, forming partnership with pharmaceutical companies, raising capital, advancing or failing in phases of development, and changes in managing teams. Biotechnology companies, especially start-ups, need to attract attention from potential investors, would-be employees, scientist community and the public. Because the biotechnology industry and community have risen to be a critical element of the local economy, the quantity and quality of journalistic writing have gradually increased. Regarding the journalistic writing, I have been aware that I look at the past events through the eyes of journalists. Journalists, according to Czarniawska (2004), write more 'emplotted' documents, which represent their interpretations of events or episodes, even though they usually employ accounts of 'insiders' in interview quotes and ‘objective’ data. I have been aware that the subjects and content of each article were selected and processed by journalists. In the opinion section, I found a large number of columns contributed by entrepreneurs, scientists and civil leaders from the biotechnology community. These contributing columns were written to deliver their points of view and concerns over local problems to deal with communal issues by communicating either with the business community or the entire local community.

At this early stage, I started writing memos on each company, entrepreneur, community initiative and program chronologically under each category. Through this step, I started perceiving the process of founding start-ups, the typical trajectory of translating science into products or processes, and the strengths and weaknesses of local environment in doing business. Each start-up company had implications to the entire ecosystem of the San Diego biotechnology industry, as an embedded element. By composing cases and accounts, I recognized the variety of business models, strategies, processes, relations, regulatory contexts, communal concerns, and interactions with other communities. Reading books and reports on biotechnology, industry and even general management were useful in locating each case in the entire picture. At the same time, interviews and other archival sources were critical to expanding my understanding, as well as to motivating me constantly. Through this process, patterns and trends appeared as more data were collected and aligned along concepts. For example, I began recognizing that a certain group of individuals tended to employ a specific set of practices – business models, strategies and ways of mobilizing resources – in establishing start-ups. Similarly, each entrepreneur tended to reuse, reutilize and revitalize their expertise and relational assets in building up a line of start-ups. Also, I found that some platforms or practices have been repeatedly employed in implementing collaborative initiatives. Constant comparing between data and iterative thinking grounded on data have been central to developing, sophisticating and revising concepts. Conversely, the concepts have been instrumental in rediscovering the meaning and relations of data.

After collecting articles in San Diego Union-Tribune, I referred to the San Diego Business Journal, which has covered business news weekly since the 1980s as a prime local business news magazine. This media provided more focused information and accounts on the local industries. Like the daily newspapers, the business and civic leaders have utilized this media extensively to raise their voices, by contributing columns on various issues. Combined and compared with articles from San Diego Union-Tribune and other archival sources, it added more dimensions to the historical changes of the local industry. In many cases, the articles in San Diego Business Journal provided additional accounts or contrary viewpoints to the newspapers. In addition to these local journals, I depended on several other periodicals: San Diego Metropolitan Magazine, North County Times, Daily Transcript, Journal of San Diego History, and Xconomy San Diego (an internet-based newspaper focusing on the technology industries.)

I have collected a substantial amount of data from several local broadcasting channels: KPBS (local PBS station), UCSD TV, SignOn Radio by San Diego Union-Tribune. At the same time, I found that several websites of trade associations and research institutions local organizations were a rich source of archival data by posting video or audio podcasts of past events like interviews, conferences, seminars, panel discussions, presentations and business competitions, along with news releases. During the early period of this research, these were an excellent window to access the community, and an opportunity to listen to the community leaders, entrepreneurs and scientists. I transcribed dozens of podcasts from these sources either partially or entirely. These transcriptions constitute an important portion of my data set.

### *3-2-2. Semi-Structured Interviews*

Story making is a universal and omnipresent process through which we shape our experience of social life, understand the meanings of the world, justify our actions, and transfer our experiences to the next generations. In this sense, a large portion of social learning occurs through narrative activity of creating, telling and listening to stories (Bruner, 2002; Czarniawska, 2004). I align with Czarniwaskwa's (2004, p. 5) point of view that "to understand a society or some part of a society, it is important to discover its repertoire of legitimate stories and find out how it evolved." I regarded the interviewees as story tellers who plot their experience and interpretation in narratives. Story represents the teller's social world; the shared story of a community shows the collective social reality.

I viewed interviews as a dynamic and interactive play, whereby an interviewer and an interviewee interact "to produce meaningful stories" (Holstein & Gubrium, 1995, p. 28). Therefore, I sought to let the interviewees tell their stories, rather than impose any structured questions. I began every interview by asking about each interviewee's past experience and current activity, and ended it by asking for any suggestions for and advice on my research. I asked interviewees additional questions on specific motives or reasons for taking action. Then, I solicited interviewees to tell their perspectives on the biotechnology community, and on some activities they were involved in. I prepared a set of questions, tailored to each interviewee's experience and engagement, prior to each interview meeting. For example, if an interviewee was a serial start-up entrepreneur, most questions revolved around her start-up activity and perspective on the local environment related to establishing and running start-ups. If she was a venture capitalist, I raised questions about her activity as an investor and perspective on the local venture capital setting. But, several questions were improvised during each interview in accord with the evolving conversation. I always tried to be responsive to the flow of interviews' storytelling rather than to impose any prepared questions. I always tried to reference the previous account to move on to the next question. For example, I responded to an account by saying, "Oh, that's very interesting. Can you tell me why you did that?" During each interview, references and cases were employed to activate story telling (Holstein & Gubrium, 1995): as an example, 'an entrepreneur told this. What do you think about her point of view?' or 'that's very interesting. Can you give me more some specific cases to support your point-of-view?'

In raising interview questions, I sought to allow interviewees to tell their stories. In the early stage of this research, the questions mostly revolved around processes and mechanisms of entrepreneurial activity or communal initiatives. Without much background, I needed to focus more on procedures and social contexts of starting up, running companies, or transferring technology from academic setting to industries. As I collected more data and spent more time analyzing them, new codes and concepts emerged gradually. To identify and articulate properties and dimensions of emerging concepts, I needed to refocus and restructure inquiries (Corbin & Strauss, 2008). As I became more interested in knowing the logic and contexts rather than logistics of activity, I began to focus more on 'how' and 'why' than 'what' and 'who' questions.

In identifying and approaching to interviewees, I drew on the "chain-referral" and "snowball sampling" methods. At the beginning of this research, I categorized potential interviewees into three groups: entrepreneurs, investors and service providers; scientists at UCSD and research institutions; directors or managers of partnership programs, trade associations, and local governments. A number of people were soon identified because they had been frequently quoted in newspaper articles, and had spoken at events. First, I requested interviews with these people by sending letters and emails to addresses found on websites. But, this effort did not bear any fruit. It was personal contacts at networking events, seminars and award ceremonies that enabled me to make appointments for most interviews. As an example, I introduced myself to a program director, and asked to have an interview. The director approved my request on the spot and mentioned that she would not respond to any email interview requests since there is no assurance of genuineness. These early interviewees referred me to their friends, or informed me of other 'insiders' to be interviewed. In some cases, they asked their associates to do an interview by sending emails, and asked them to help me. Some of them introduced me to their friends at social events. Some of them permitted me to mention that I did an interview with them in requesting interviews with their friends or peers. It was rapport and relationship, that let me access a majority of interviewees (Feldman, Bell & Berger, 2003). So, at this phase, the chain-referral or snowball sampling was the main sampling method (Lofland, Snow, Anderson & Lofland, 2006).

In the process of conducting interviews and analyzing data, I identified a number of individuals to be interviewed to reinforce and validate concepts in development. Subjects were identified and selected in relevance to conceptual frameworks, thus 'theoretical sampling' was the primary method for the late part of this research (Glaser & Strauss, 1967; Corbin & Strauss, 2008). These people included key actors, who established and ran important companies, contributed to developing communities for learning, and played pivotal roles in community initiatives. I made a list of these people, and sought to contact them through two methods: I went to certain events where these people on the list were supposed to attend as keynote speakers or panelists, and I asked interviewees to refer me to these people. In asking for references, I utilized my knowledge of the relational networks of the local community from archival data and previous interviews.

Through these efforts for two and half years, I have completed 43 interviews with serial entrepreneurs, managing executives, academic scientists, investors (venture capitalists and angel investors), public officials, program directors, and practitioners in specialized service sectors. Most interviewees have been involved in a variety of activities at multiple organizations. Along their career paths, they have been successful with some endeavors, but usually, they have experienced failures in some efforts. Many entrepreneurs whom I interviewed have established a series of start-ups, and they have experienced ups and downs in the process. Virtually all entrepreneurs and investors have relationships with academic scientists, particularly, at UCSD and research institutions in La Jolla. Some entrepreneurs used to be faculty, post-doctoral fellows and graduate students at research institutions. For example, I did an interview with a director of business development at Sanford-Burnham Institute. He had built a company in the early 1980s based on his research at UCSD, and was actively involved in founding three more start-ups before joining Sanford-Burnham Institute. I did interviews with first-time entrepreneurs, who were either still in a Ph.D. program, had just finished a post-doctoral fellowship, or were done with their doctral degree. I met them at business competitions or networking events, in which they were participating to gain 'visibility' and develop 'networks'. I did several interviews with academic scientists, who had engaged in commercializing activity by establishing start-ups or collaborating with established companies. Each interview gave a quite different perspective, but the diversity and difference were fundamental to developing theoretical concepts.

During the first year, I did all interviews face-to-face for about one hour. However, in the late stage, about a dozen interviews were done by telephone for about 30 minutes. I did several follow-up personal communications by emails to ask a few more questions, which had been missed during interviews or emerged after interviews. It was after about 30$^{th}$ interview, when I began to perceive “theoretical saturation,” that refers to a point in time at which no more concept or property of categories is found from new data (Glaser & Strauss, 1967). For example, in explaining their logics and contexts of entrepreneurial activity, they referred to a set of enabling or constraining factors, which revolved around theoretical concepts like learned skills and relationships. In accounting for robust start-up activities and collaborations in San Diego, virtually all interviewees pointed to a set of elements including dynamic interactions between groups of entrepreneurs, educational programs and CONNECT. Although I believe the number of interviews was above the threshold for validating concepts, it was a negotiated result in consideration of my limited time, capacity and resources. Every individual took his or her own path, and developed a unique perspective, therefore each interview helped me understand and construct concepts.

A series of procedures for each interview, which included requesting interviews by emails, meeting, transcribing, memoing and rereading, was instrumental to generating categories and formulating theoretical frameworks. It was the interviews that reoriented research foci and nurtured theoretical concepts. All interviews except one were tape recorded and transcribed – one interviewee simply refused to be tape recorded. In transcribing, I looked up information sources to understand narratives or to write down names of people and companies. I added questions or clipped references after some paragraphs. To me, transcribing each interview was the most stimulating and productive process. I wrote analytical memos at the end of transcribed interviews in hope of identifying and developing concepts. As an example, in answering the first question – ‘tell me about your career or experience’ – the interviewees told the meanings of experience as well as information on it. They told me why and how they had taken certain actions under what contexts. By juxtaposing and categorizing interviewees' trajectories and explanations of activity, I identified concepts like 'developing identify as entrepreneurs', 'learning by doing', 'learning by interacting', and 'knowing through practicing'. Along with archival data and field observations, the interviews were critical component to developing concepts in the dissertation.

### *3-2-3. Field Observations*

One of the most exciting and productive moments of this research was ‘being there’ while attending social and educational meetings. These were the main channel whereby I accessed a number of people, and came across 'Aha' moments. Being in the field with the people helped me understand how the local community is constituted, and how the local people experience and interact in real situations. All year around, trade associations and research institutions hold many networking meetings, workshops, seminars, business competitions, educational programs, financial forums and award ceremonies. Most events are open to the public, and they were even free or discounted for students. The first event attended was a panel discussion – *Creating companies from emerging technologies: Perspectives from Cambridge, Menlo Park, and San Diego* – in February, 2008, and the last event was CONNECT’s 25$^{th}$ Anniversary Celebration in June, 2010.

I took advantage of every attendance to build rapport with other participants and to develop concepts. As an example, I twice attended an awards ceremony, *Most Innovative New Product Awards (MIP)*, which has been held annually by CONNECT to recognize the endeavors and contributions of the community members, in 2008 and 2009. There, for the first time, I had an unforgettable experience, which was jotted in a field note: “when I came back to the exhibit hall, I could hear nothing except 'buzzing' sound. The hall was full of people, and everybody there was talking to somebody.” I was impressed by the warm and intense atmosphere of the gathering. During the second attendance, the experience was quite different: At the event, I came across several interviewees to whom I expressed appreciation for their interviews and shortly explained what was going on with my research. One of them said, 'how can I help you?', and introduced me to a director of a program on-the-spot. By attending the same event twice, I perceived that the repertoire of the second year's event was virtually identical to that of the previous year. In the field note, I wrote: “the pamphlets of two events tell and show the same stories. The foci were both given to the founding fathers of CONNECT, and the dedication of William Otterson, founding director of this program.”

I experienced several 'Aha' moments while I was in the field listening to and talking to many participants. For example, many interviewees pointed out that the San Diego biotechnology community is more collaborative than any other region: entrepreneurs can easily work with academics, academics can access entrepreneurs, multiple organizations have successfully done many initiatives; however, I was struggling to explain the culture of collaboration. A concept to explain the culture of collaboration came out when I was attending a panel discussion, where I listened to an academic scientist telling about collaboration: “The primary challenge is how actually we make progress. Then you *figure out* how to formalize collaboration, how we formally work together" (emphasis added). His remark helped me construct a concept to understand collaborations: effective collaborations take place when participants share practices, rules, goals and values; to share practices and understanding, individuals need to engage with partners in the process of solving problems and resolving conflicts.

As another example, I was sitting listening to start-up entrepreneurs pitch their business plan at a competition – *the 3rd UCSD Entrepreneur Challenge of 2009* – which had begun in 2006 by a student-run organization to elicit and nurture entrepreneurship among UCSD students. Five final teams, who presented their business plans at the event, had gone through a year-long process to be the finalists out of 70 applicants. By reading a pamphlet and navigating the event's website, I knew that the participating teams had been trained, connected and mentored in the process: business competitions provide a training and networking platform for newcomers. However, by sitting in the audience, I discovered more dimensions to this event. First, would-be entrepreneurs gain 'visibility' by pitching their plans to many people. There were a few hundred people, from high school students to elderly in their 70s or 80s, in attendance. Second, I recognized that the business competition provides educational opportunities to the audience too. I talked with a young researcher at the Sanford-Burnham Institute. I found that it was her second attendance, and she was interested in founding a startup: she came to learn how to make business plan and what resources start-ups draw on in the early stage. Another experience enhanced this recognition. Next to me, a senior and a junior scientist from Sanford-Burnham Institute were talking to each other throughout the event. For each presentation, they made notes, and conversed. When a presenter pointed out patent licensing as one of their revenue sources, the junior person asked the senior about it to the senior person.

It was not only listening, but also many short, informal conversations with participants at events that helped me expand my understanding. Upon hearing my research topic, many people did not hesitate to give their perspective, mostly by referring to 'Hybritech', ‘CONNECT', 'UCSD' and a culture of collaboration. Some told historical episodes and some named people to be interviewed. By walking around the Torrey Pines Mesa area, I encountered many artifacts of photos, renderings and symbols displayed in the offices or halls of trade associations and research institutions. Driving and walking around the area were crucial to understanding the geographical composition of the community: where biotechnology companies and research institutions are located; in which built and natural environment they work. In these ways, field observations greatly supplemented archives and interviews by allowing me to get in touch with people, listen to stories and experience space.

### ***3-2-4. More Notes on Analysis and Writing***

In this last section, I explain how I compared data from multiple sources, and integrated writing with the processes of literature review, data collection and data analysis. As the first step, I chronicled data of biotechnology companies, people, programs and events. The data from multiple sources helped me piece together what has happened to this community since the early 1980s. In seeking to capture the whole picture of each episode, the data from different perspectives, time points and sources were juxtaposed. For example, the scientific and industrial leaders sought to locate the headquarters of California Institute for Regenerative Medicine around 2002. Any one piece of data either from interviews or archives did not contain the details sufficiently telling what went on, who led the initiative and why they embarked on the imitative. By reading and comparing dozens of articles from several sources and interviews, I perceived the motivations and process of the initiative. It was another episode telling how I knew about interactions between seasoned and novice entrepreneurs. I was curious about how the many educational and mentoring programs in San Diego help novice entrepreneurs, and why seasoned entrepreneurs share their expertise and experience with newcomers. By listening to stories from both mentors and mentees, I could understand what makes the two sides interact.

From the beginning of this research, I wrote memos or drew diagrams as a way to identify and develop theoretical concepts. These were written in forms of long or short memos, diagrams, taxonomies, flow charts or jottings. Gradually, concepts have become articulated and sophisticated as I collected more data and spent more time discovering patterns and trends in the data. As new concepts and categories emerged, many of the early memos and outlines became meaningless. In developing concepts during the early stage, I drew on the literature about industrial clusters and technology transfer: the literature provided a set of elements or factors, that facilitate or constrain the development of industrial clusters or that of academia-industry relationships. In addition to the literature, speeches and writings by leaders of the local community at lectures, seminars and newspaper columns helped me perceive how the insiders explain the development of their biotechnology industry. Commonly, they ascribed the dynamics of the San Diego biotechnology industry to several factors: existence of outstanding research institutions, availability of early-stage capital, a large pool of management talent and a culture of collaboration. On the contrary, during the late-late stage of this research, the literature on organizational learning, communities of practice and embeddedness of economic activity was a fundamental component in developing theoretical concepts, along with interviews.

While collecting and analyzing data from various sources, I have always looked for any quantitative data which would have implications to the research questions. Especially, I wanted to collect longitudinal data showing long-term trends of the development of the biotechnology industry and research institutions. During the last two years, I contacted a number of institutions, like the NIH, the California Labor & Employment Department, San Diego Association of Government (SANDAG), San Diego Regional Economic Development Corporation (SDEDC) and the City of San Diego. Some of these data have been fundamental to reorienting my research focus and developing concepts. A data set of NIH grants awarded to research institutions in San Diego reoriented the ongoing research focus. Initially, I presumed that the scale of the local commercial activity would be proportional to the amount of the NIH research funding granted to research institutions in San Diego, but the data showed that the percentage of the NIH funding flowed to San Diego has remained constant, while the industry has expanded its activity to be one of the top biotechnology clusters in the country (refer to Table 4-2). This observation resulted in turning attention to the local context of commercial activity.

I was most excited when I found fits between collected data and theoretical concepts from the literature. I had to struggle with the data for several months before discovering theoretical concepts or frameworks to piece data together. It was an iterative process of inquiry moving between data analysis and critical reading of the literature. By juxtaposing data with theories, I found new dimensions and properties in the data. Therefore, theories and the literature enabled me to construct storylines, combine data and figure out how each piece and set of data could be linked to each other; but on the other hand, the process of collecting and analyzing data was critical to understanding the significance of theoretical concepts from the literature. In the end, this research involved the interactions between data from multiple sources, theoretical concepts from the literature and personal experience in the field.

# CHAPTER 4: GENESIS AND EVOLUTION OF THE COMMUNITY

## 4-1. Early Economic Landscape of the San Diego Region

Until the recent decades, San Diego was acknowledged as an isolated territory overshadowed by the Los Angeles metropolitan area. In the late 19th century, it was Los Angeles in Southern California that was connected to the east by the transcontinental rail system. It also built the most efficient cargo handling system in its harbors. People and cargo were transported to San Diego en route to Los Angeles. Heiges, Stutz, and Pryde (1984, p. 154) described the geographical remoteness and lack of connections as follows:

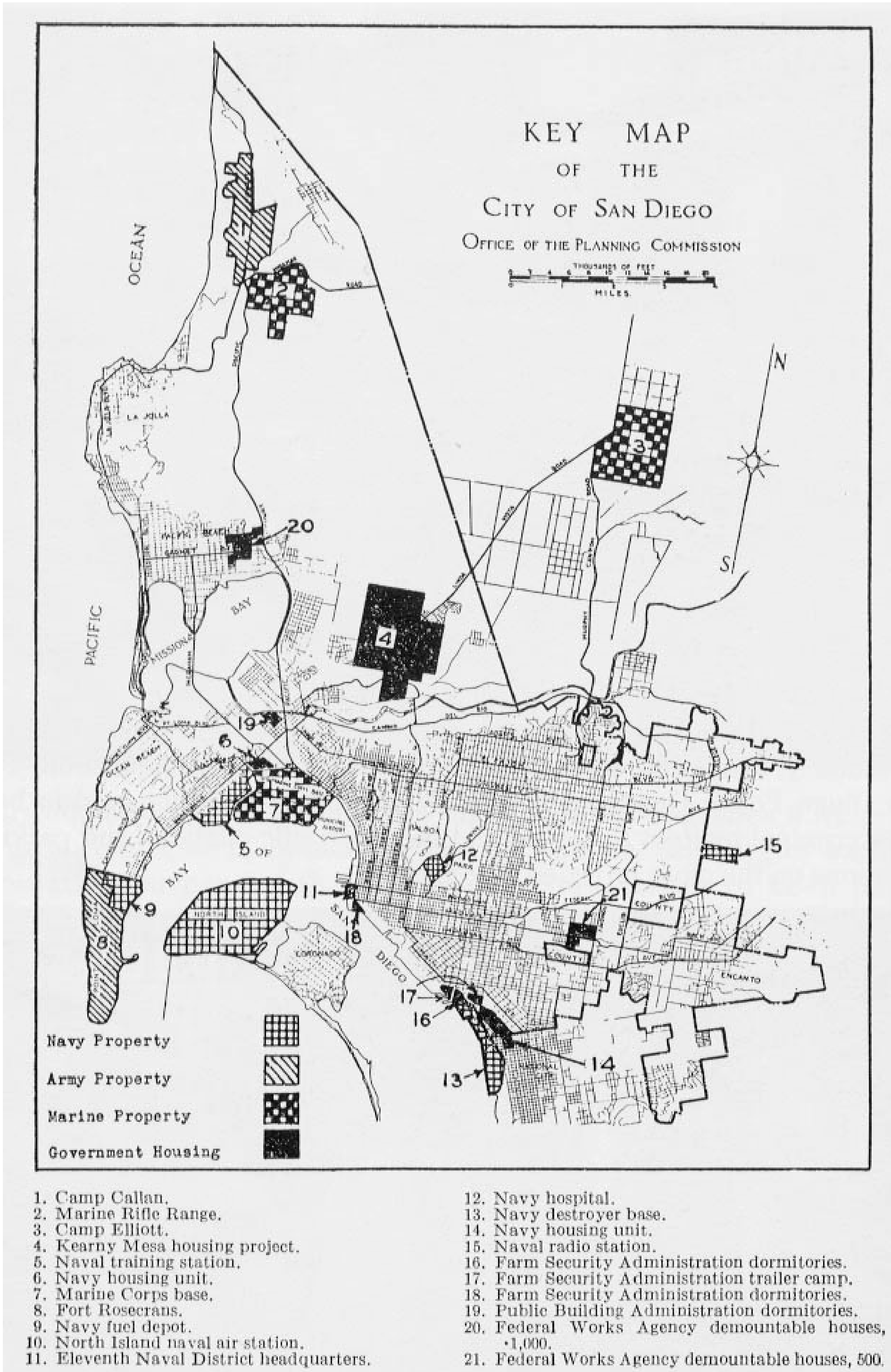
> San Diego's relatively remote situation has had a negative influence on its economic development. Trade is restricted to the west by the Pacific Ocean, to the south by the international boundary, to the east by the Peninsular Ranges, and to the north by the economic dominance of the Los Angeles Basin.

In this sense, San Diego was called a 'cul-de-sac' of California, which referred to the geographic and economic isolation of this region from the main part of the country. San Diego also lacked material resources necessary to launch heavy industries, as well as any significant tradition to develop manufacturing industries to a significant level on its own effort (Heiges, Stutz & Pryde, 1984; Stutz, 1992). Prior to the 20th century, the local products ranged from agriculture to mining and fishing. Tourism began to grow from the late 19th century when this region was served by the California Southern Railroad in 1885, and the Hotel del Coronado was built in 1888 (Stutz, 1992). The weather of Southern California and the pristine environment lured a retiree population along with tourists. People migrated to San Diego to retire or to serve those retired. Until the coming of Navy and an aircraft manufacturer, Convair, during World War II, the most pivotal economic component was housing developments for retired Midwesterners, which inevitably involved ‘booms and busts’ (Davis, 2003). As Davis (2003, p. 27) noted, “the city’s boom economy seemingly consisted of speculators selling land to other speculators.” Until the early 20th century, San Diego was known to outsiders as a vacation spot under the sunshine of Southern California. Heiges et al. (1984, p. 154) described the economic landscape: "Prior to 1920, San Diego County was primarily agriculturally oriented, except for the coastal strip which was dotted by resort communities stretching from Coronado to Carlsbad."

The United States Navy began to build facilities in San Diego from the early 20th century, mainly attracted by the climate, abundance of land and its natural harbor. Among the first permanent facilities of the United States Navy was a naval coaling station on Point Loma at the beginning of the 20th century. This facility resulted in increased visits of Navy ships to San Diego. In 1906, the first power radio station on the West Coast was built in San Diego (Driese, 1992a). The Navy constructed a destroyer base on the San Diego Bay during 1920s. The climate allowed the Navy to take advantage of "open air storage, reduced heating costs, and almost year-round test flights" (Stutz, 1992, p. 156). The climate advantage and the presence of the Navy brought in the aircraft industry. The early aircraft builders include Ryan Aeronautical Company and Consolidated Aircraft Corporation (Convair), which merged with General Dynamics in 1953. Aside from this modest growth in defense industry, San Diego was mainly a destination for retirees prior to World War II.

During World War II, the Navy and Marine Corps built a number of military bases and camps for training and housing military recruiters in the region. By the end of the war, significant part of the city was appropriated by the military as shown in Figure 4-1. Camp Callan (1) was transferred to the City of San Diego in 1946 and is the main location of the biotechnology cluster, and Marine Rifle Range (2), which was also called Camp Matthews, was transferred to UCSD to be part of the campus. Between 1940 and 1944, the size of the city population doubled with the influx of 165,000 defense 'migrants' who were employed by the defense plants (Anderson, 1993). At Convair, which had moved to San Diego in the mid 1930s, there were 45,000 workers to produce planes at its height in 1943 (Eddy, 1993). After the war, San Diego became one of the world's largest Navy bases, where current and retired servicemen constituted a large part of the local population and a significant part of local industries were based on the defense sector. Still, San Diego had remained 'a sleepy Navy town' until it unfolded itself as a hub of the biotechnology and telecommunications industry by the late 1980s or the early 1990s.

**Figure 4-1.** Military presence during World War II




*Source*: Eddy, 1993.

San Diego's economic growth during the Cold War came from a group of skilled people, many of whom were servicemen returning to San Diego where they had been trained. Along with aircraft manufacturers, a group of electronic companies were spawned from the skilled talent in the defense industry. By the 1980s, San Diego's economy was largely based on manufacturing, defense and tourism. For example, in 1982, the defense industry was the source of 355,000 employees, and it accounted for 16 percent of Gross Regional Product (GRP) through payrolls and contracts (Bauder, 1984). In evaluating the impact of the defense budget on the local economy, an economist said that the military "represents a leg and a half" out of three legs (Bauder, 1984). In 1984, a report estimated that the military spending accounted for about 20 percent of GRP by adding $6.5 billion, and one out of five people in San Diego County was employed in or by the sector (Riggs, 1985). The defense expenditure paid contracts for shipbuilding and repairing as well as buying aircraft, electronics and goods of local businesses. General Dynamics Corp, Cubic Corp, and Science Applications were the three largest contractors among 1,200 businesses in 1984. Linkabit, the precursor of Qualcomm and the telecommunications industry in San Diego, was founded and grown by taking advantage of the defense expenditures. These companies became the seedbed of the local electronic, telecommunications and other high technology industries.

## 4-2. From the Scripps Institution of Oceanography to UC San Diego

The defense contractors, particularly General Dynamics Corp, needed an educational and research university for anchoring and training their skilled employees. And the pristine land on Torrey Pines Mesa, a large part of it was abandoned military bases, provided opportunities for the City of San Diego to build scientific institutions. The three main research institutions in San Diego – UCSD, the Scripps Research Institute (TSRI) and the Salk Institute for Biological Studies (the Salk Institute) – came to La Jolla between the late 1950s and the early 1960s. The University of California's Board of Regents officially approved a new UC campus in La Jolla in 1959 and UCSD embarked on its undergraduate programs in 1964 (Shragge, 2001). TSRI recruited Frank Dixon, a prominent immunologist, and his colleagues in 1961, who established the Department of Experimental Pathology. Jonas Salk, developer of the polio vaccine, began to build a research institute on 26 acres of land on a seafront bluff that had been gifted from the City of San Diego in 1960.

The first scientific institution in San Diego is the Scripps Institution of Oceanography, and this institution was fundamental to attracting or constructing UCSD and biomedical research institutions. Even though the opening of a fully fledged campus of University of California came in 1960, the seed of UCSD was sown in the early 1900s with the Scripps Institution of Oceanography. William Ritter, a professor of zoology at the University of California, Berkeley, envisioned a world-renowned biological station in San Diego with support of a local physician, Fred Baker (Shor, 1981). Fred Baker invited William Ritter to San Diego and secured the commitment of the San Diego Chamber of Commerce. To establish a lab, he also raised $500 from Edward W. Scripps, newspaper tycoon, and Ellen B. Scripps, sister of E. W. Scripps in 1903.  In 1907, E. W. Scripps chose an undeveloped site at the La Jolla Shores beach and bought the parcel from the City of San

Diego. On this site, the first building was constructed in the following years. (see Figure 4-2.)

**Figure 4-2.** Scripps Institution of Oceanography, 1911

*Source*: Cuthberth, 1980.

In 1912, the institution was transferred to the University of California, and the Regents renamed it the Scripps Institution for Biological Research in recognition of Ellen B. and Edward W. Scripps. In the early period, most of the funds for facilities and research activity came from Ellen B. Scripps. In the midst of expansion in 1920s, it was renamed 'the Scripps Institution of Oceanography'. This institution, as shown in Figure 4-2, had remained isolated until the establishment of UCSD in La Jolla.

It was in the 1950s when a group of people initiated a series of efforts to establish a university. The institution provided a teaching program to graduate students along with research programs. Roger Revelle, director of the Scripps Institution of Oceanography from 1951, and faculty were concerned about poor performance of their graduate students at the institution. To them, this institution was an isolated research and graduate education laboratory of the University of California lacking the needed interactions with and exposures to the whole body of academic community. They sought to turn the institution into a full-fledged research campus, as Revelle (1974[1991]) remembered:

> We thought this was due in large part to our own narrow specialization and to the lack of an atmosphere of fundamental science in La Jolla. It seemed to us that we could overcome our difficulties by an academic invention: creation of a graduate school of science and engineering - a kind of publicly supported Caltech - located as near as possible to the Scripps Institution.

At the same time, the local government needed a new source of economic activity, so they turned their attention to nuclear and newly emerging defense technologies. But, these industries needed a research university, which attract and train skilled employees. After World War II, local manufacturers of aircraft and airplane struggled to survive. Many of them were sold or forced to downsize as the defense budget decimated. At the end of World War II, the city experienced more than a 90 percent drop of production (Anderson, N., 1993, p. 38). During the turbulent and anxious years, those technology-based industries and the city welcomed the idea of establishing a nuclear research campus in La Jolla proposed by John Hopkins, president of General Dynamics. The city donated 120 hectares of land in 1955 to the company, in which they built a research facility of General Atomics. Soon, the people at General Atomics realized that they should have a university campus anchoring and training a pool of scientific and engineering talent. In

1956, General Dynamics pledged to donate $1 million to the regents, given the university would keep expanding a School of Science and Engineering that had been just approved by the regents in its resolution ("University of California, La Jolla", 1959).

Mayor Charles Dail, elected in 1955, envisioned and pursued building up a new employment base on Torrey Pines Mesa (Bourgeois & Eckhart, 2009). The city was watching the growth of employment at General Atomics, and it owned large amounts of land – Camp Callan had been returned to the city in 1946 and left largely abandoned – for future development. A state assemblyman, Sheridan Hegland, in working with Ravelle, proposed a House Resolution asking the Board of Regents to review the appropriateness of establishing a new UC campus in San Diego in 1955 (Deerlin, 1985). Following this legislative initiative, a group of academic and industrial leaders took steps to persuade the State government and the regents. The city council voted to give "certain City-owned lands" to the university in 1955 (Anderson, N., 1993, p. 40), and the ballot proposition, Proposition D, was passed to empower "the City Council to give the University of California some 450 acres of pueblo lands on Torrey Pines Mesa in 1958 ("University of California, La Jolla", 1959).

The Sputnik shock of 1957 was the turning point for dramatically changing the attitude of the public toward research and development of the public, and the commitment of the federal government to science. In this period, California was experiencing rapid growth of population, and this demographic change brought in more demands on higher-education service. In 1958, the regents approved the establishment of a School of Science and Engineering in La Jolla. A committee at the University of California brought up an idea of establishing three new full-fledged campuses in San Diego, Orange County and Santa Cruz. In 1959, the regents finally approved the establishment of a campus in La Jolla. The University of California was still under a negotiation with the federal government to have an adjacent Navy camp of about 500 acres, Camp Matthews, be transferred to the new campus. The camp, which would comprise 1000 acres of land combined with the city gifted parcel, was transferred to the university by 1964.

From the beginning, Revelle and founding members sought to "create an instant great university" by recruiting renowned faculty and emphasizing research (Revelle, 1969). To achieve this goal, the founders, including Revelle (1974[1991]), started to build graduate schools first:

> We decided to do just the opposite - to build our first "little university" from the top down, or, if you like, to lay the roof first. We started to build a series of graduate research and teaching departments, one at a time, first in physics and chemistry, then in the earth sciences and biology… In each department, we aimed for a critical mass of faculty who would be able to give doctoral programs right from the start. This was a crucial decision, because it was one of the prerequisites for assuming that our first faculty members could be outstanding scholars and researchers. As such, they would be largely self-supporting, in terms of research and training grants.

Revelle went to, first of all, the University of Chicago and succeeded in attracting Harold Urey, Nobel laureate chemist, to La Jolla in 1958. Revelle said regarding the joining of Harold Urey: "the coming of Harold Urey in 1958 gave this concept credibility" (Revelle, 1969). Soon, Urey's colleagues including James Arnold and William Libby joined the new campus. On the side of biology, Revelle successfully attracted David Bonner from Yale University (Anderson, N., 1993). The recruited faculty brought in research funding, graduate students and reputation as well as capabilities. The coming of prominent scientists led to another wave of arriving scientists. Jonathan Singer (Atkinson & Singer, 2009) , an early arriver and one of founding members of the Biology Department of UCSD, attributed the upstart of UCSD to the success of recruitments and high enthusiasm of early arrivers.

> People who arrived here early were not only brilliant, with some exceptions. But almost everyone had a tremendous sense of judgment about people and their qualities… I should say that I know at least ten of the people who were very active in those years who had this fantasy that they had the chance to build a university, a research university, second to none in the country. They were convinced of it. I was. And, it was a great thing to be convinced of even though it was, it turned out naturally to be a fantasy. But it always impelled all of us to not be satisfied with what might be happening.

Revelle and founding members envisioned heaven in La Jolla for academic research as Caltech in Pasadena. The founding members were enthusiastic in establishing an outstanding research university which would give the priority and privilege to research of faculty. Until the 1980s, the university had been busy in building up an ivory tower, without much attention to their local neighbors. Faculty needed to pay attention to peer review process of federal agencies to maintain and expand their research enterprise. Moreover, until the 1980s, the faculty members were not exposed, to a significant extent, to the endeavor of the private sector. To most scientists at UCSD, entrepreneurial activity was still foreign to their everyday laboratory life.

### 4-3. Expansion of Scientific Base on Mesa

The origin of the Scripps goes back to Ellen B. Scripps's founding of the Scripps Hospital and the Scripps Metabolic Clinic in 1924. She was interested in studies of metabolism as well as marine biology (Carlson, 1978). In 1946, the Scripps Metabolic Clinic was renamed the Scripps Clinic and Research Foundation when "a major portion of the Clinic's limited reserves were committed to the construction of a new research facility and to the recruitment of top biomedical scientists" (Scripps Research Institute, 2010).

The critical step to being a prominent research organization was its recruitment of Frank Dixon, an immunologist, and four of his colleagues from the University of Pittsburgh in 1961. They came to the institution to engage in their research without any bureaucratic intervention. Frank Dixon founded the Department of Experimental Pathology at the Scripps Clinic soon after he had arrived in La Jolla, and he headed the research division until 1986. What attracted Dixon and his colleagues to "basically a small-town hospital with an allergy clinic" in La Jolla was the freedom to do research full-time (Maugh II, 2008). Michael Oldstone (2008), Dixon's postdoctoral fellow, wrote:

> His vision was to concentrate whole, independent laboratories researching experimental models of human disease. This goal led Dixon to seek a place where he and his faculty could pursue research undisturbed by the necessary university business of administration, teaching and patient care. It was in this climate that Dixon and four other experimental pathologists from the University of Pittsburgh Medical School moved to the then remote hamlet of La Jolla, where they accepted an invitation from a small and financially limited Scripps medical clinic that offered no institutional barriers to full-time research, provided it paid its own way.

The scientist group wanted a place where they could commit their time and energy to the emerging field of biological studies. There was no salary at the Scripps Clinic and Research Foundation, so the scientists had to raise their own salary and research funding mostly from the National Institutes of Health (NIH). These early arrivers set up an institutional setting of scientific enterprise, and their work and reputation played a crucial role of attracting scientific talent as well as enhancing research capacity. Charles Cochrane (Scripps Research Institute, 2003) recounted how he and the cohort worked in the early 1960s:

> We laid down a basic foundation in the institute that promoted maximal freedom for the scientists to pursue their individual interests unfettered by committees and regulators. Then we all went to work to put the institute on the map, through publications and presentations at national and international meetings. We were looking at a future that was undetermined - a horizon beyond our scope of imagination.

The scientists at the Scripps were able to decide where to commit their time and energy on their own, but they were under constant pressure to secure grants from, mostly, the federal agency. Oldstone (Cochraine & Oldstone, 2009) described it this way: "Your salary is dependent on the grant support you raise. The concept of Frank's was what we call "scientific Darwinism." It was that you selected people who wanted to do research full-time, and they could stay as long as they wanted to do research." As a consequence of these efforts, Cochraine (Cochraine & Oldstone, 2009) noted, "everything began to grow… Our rate of growth was doubling every four years."

The Salk Institute came to San Diego lured by the Mayor Charles Dail's offer of land on a sea cliff. Jonas Salk, who developed the first polio vaccine in collaboration with his research team at the University of Pittsburgh, garnered a pledge of funding from the

March of Dimes in founding a new research institute. Salk envisioned a space where scientists could study to understand human beings by integrating studies in biology side-by-side humanities (Academy of Achievement, 1991). He traveled around the country to choose a location for the institute. Charlis Dail, major of the City of San Diego, invited Salk to San Diego, and offered a 26-acre site on the cliff of the La Jolla Mesa in 1960. Lured by the land and the fledgling UCSD, the Salk Institute was incorporated in 1960, and started operating in 1963 on the gifted site (Bourgeois & Eckhart, 2009). The founding faculty consisted of a group of renowned scientists including Francis Crick, the discoverer of the structure of the DNA molecule in 1953 and Jacques Monod, director of the Pasteur Institute from 1971 to 1976 – both of them were Nobel Laureates. These people brought in groups of scientists to the institute as a way to create a chain reaction.

The coincidental formations of three research institutions – UCSD, TSRI and the Salk Institute – brought in a wave of scientists full of ideas and energy. One of the early arrivers, Cochrane (Cochraine & Oldstone, 2009), remembered the atmosphere in the early 1960s:

> [A]ll around us were people who were fabulous scientists from various different walks of life. And, the science was immense. The people were all young. They were involved to the hilt in what they were doing, and nothing else. They did nothing else. And, that's where Dave Bonner came forth because the Medical School, to him, was a scientific school essentially. And, at the same time, in the background of this, was the National Institutes of Health, which was, at this point, putting money out for any scientist who came along, who could be judged by the merit of his work. And, this made the whole thing flower even further.

UCSD, TSRI and the Salk Institute leveraged the presence of neighboring institutes in luring talent and funding. The tradition of collaborations between the research institutions in La Jolla goes back to the 1960s, when they began laying down their foundations - physical facilities and recruitment of talent. The founders and early arrivers convened to share their ideas on doing research and building up institutions. The research institutions on the Mesa incorporated a variety of collaborative initiatives including endowments of joint positions. Cochrane (Cochraine & Oldstone, 2009) recounted the rise of collaborations between the three research institutions:

> We got to know these people and we decided the best thing we could do would be to have meetings together so we could discuss our science and where we were going and how to build the three institutions... The groups that met together were the harbinger of events in the future and as the institutions grew, we got to know people in each faculty better. We shared faculty appointments, in fact. We would have research grants together and interests in common, have meetings together in the various institutions. You can imagine the germination of ideas that came from all this mixed talent.

More importantly, the growth was possible due to the expanding NIH funding and its peer-review system. High-expectation of the public on the biological research and political consensus scaled up the NIH funding on academic research almost every year (see Table 4-1).

Riding on the rise of funding from the federal government and rapidly expanding stock of science on biology, several new scientific institutes were started. In 1976, William H. Fishman, former director of the Tufts University Cancer Center in Boston, founded the La Jolla Cancer Research Foundation, which would be renamed 'Burnham Institute for Medical Research' and recently 'Sanford-Burnham Medical Research Institute' (the Sanford-Burnham Institute). He came to San Diego attracted by the ambience and the robust interactions between the triple institutions (Williams, 1995).

The La Jolla Institute for Allergy & Immunology was founded in 1988 with an aim of collecting immunologists under one roof. In 1990, a group of scientists including Ivor Royston, co-founder of Hybritech, established the San Diego Regional Cancer Center – it was renamed later the Sidney Kimmel Cancer Center. The founders intended to facilitate the development of cancer treatments by letting researchers work closely with clinicians.

**Table 4-1.** Historical NIH appropriations

($ billions)

| Year | NIH Appropriations | Entire Federal Budget | NIH Appropriations % of Federal Budget |
|---|---|---|---|
| 1970 | 1.1 | 195.6 | 0.54 |
| 1975 | 2.1 | 332.3 | 0.63 |
| 1980 | 3.2 | 590.9 | 0.54 |
| 1985 | 5.1 | 946.4 | 0.54 |
| 1990 | 7.6 | 1,253.1 | 0.60 |
| 1995 | 11.3 | 1,515.9 | 0.75 |
| 2000 | 17.8 | 1,789.2 | 1.00 |
| 2005 | 28.5 | 2,472.2 | 1.15 |
| 2009 | 30.5 | 3,107 | 0.98 |

*Data Source:* NIH Appropriations in U.S. are from Appropriations History by Institute/Center (1938 to Present) by National Institutes of Health, Office of Budget. Retrieved from http://officeofbudget.od.nih.gov/approp_hist.html.
Federal Budget Outlays are from (Federal) Historical Budget Data by Congressional Budget Office. Retrieved from www.cbo.gov/gudget/historical.shtml.

Scientists at these non-profit research institutions including TSRI and the Salk Institute, have been more independent, less interrupted with work besides research relative to members at research universities. They have grown to be prominent entities by recruiting prominent scientists and learning from one another. They rely mostly on human talent, not on large endowment or century-long reputations. Thus, these institutions focused more on creating the best atmosphere for scientific enterprise without bureaucratic interventions, and they were active in recruiting renowned scientists. Recently, the Sanford-Burnham Institute scouted Stuart Lipton as director of the Neuroscience and Aging Center, and Evan Snyder as director of the human embryonic stem cell program both from Harvard University. In luring the top scientists to San Diego, John Reed, CEO of the Sanford-Burnham Institute, emphasized their non-bureaucratic structure of the institute. Snyder said of Reed: "he told me to imagine the [Sanford] Burnham [Institute] as a company and our product would be papers and grants. He told me that everything around here is geared to allow you to make more product. And it is completely true" (Somers, 2006d). The scientists then brought in research funding, mainly NIH grants, more talent, and consequently competence and reputation for each institution. The largest five research institutions in San Diego brought in $707 million from the NIH in 2009, as shown in Table 4-2. In the same year, the total NIH funding granted to the research institutions and companies in San Diego accounted 2.7 percent of the agency's appropriations.

**Table 4-2. NIH funding granted to primary research institutes in San Diego**

($ thousands)

| Fiscal Year | UCSD | TSRI | Salk Institute | Sanford-Burnham Institute | San Diego State U. | Sum of 5 institutes | Total NIH funding granted to S.D. (%) |
|---|---|---|---|---|---|---|---|
| 2009 | 366,943 | 206,872 | 39,470 | 67,550 | 25,877 | 706,712 | 797,218 (2.7) |
| 2005 | 309,417 | 213,209 | 52,655 | 64,680 | 19,249 | 659,210 | 815,748 (2.9) |
| 2000 | 190,542 | 138,848 | 40,789 | 29,898 | 12,431 | 412,508 | |
| 1995 | 133,969 | 84,786 | 24,986 | 15,021 | 9,237 | 267,999 | |
| 1990 | 103,132 | 58,183 | 20,403 | 8,897 | 5,652 | 196,267 | |
| 1985 | 62,129 | 35,530 | 16,871 | 5,597 | 1,517 | 121,644 | |

*Note:* The entities in San Diego were identified by their zip codes between 91901 and 92199, and the grants of each entity in San Diego were summed.
*Data Source*: NIH Appropriations - National Institutes of Health, retrieved from http://officeofbudget.od.nih.gov/approp_hist.html
Grants given to entities in San Diego County - National Institutes of Health, retrieved from http://report.nih.gov/award/trends/FindOrg.cfm.

## 4-4. The University Community Plan: Invention and Evolution of Land Use Planning

Besides the expansion of the NIH funding, land use planning and environmental amenities in La Jolla were also critical to attracting talent and expanding research capacity. Moreover, the land use planning has been an instrumental component in the development of biotechnology industry in San Diego by facilitating interactions and knowledge transfer. A majority of biotechnology companies is located in Torrey Pines Mesa (refer to Figure 4-8). This area is bounded by the Torrey Pines City Park and Torrey Pines State Reserve on the west and northwest, Sorrento Valley on the north and the UCSD campus and Scripps Hospital on the south (City of San Diego, 1983, p. 81). Part of this area is designated as the Scientific and Research Zone in which only research related and supporting facilities can be located. Most of the entities in the Scientific and Research Zone are life sciences companies and research institutions. The proximity and campus-like environment have been critical to stimulating interactions and innovation (Gibbon, interview).

The University Community Plan was initiated in a request from the University of California. But it was city and civil leaders who invented and implemented the idea of creating a life science hub around the university. The city was observing the growth of Stanford Research Park in the Bay area and the research facility of General Atomics. Furthermore, the planning laid down the spatial foundation for people to interact, interchange and intermingle with colleagues in person. Many biotechnology companies and research institutions could succeed in part "because they can see, hear and feel what is going on" (Gibbon, interview). The natural and created environment on the Mesa has been pivotal in bringing in best talent, institutes and enterprises around the world. The density, proximity and environment amenities of the community have been critical to stimulating innovations and adaptations. A scientist (Aguilar, Z., Quoted in Broderick, 2007) described the environs of the community:

> I couldn't be happier. This is a very attractive place to develop drugs, because of all the intellectual stimulation we can get from the scientific institutions around here. In that regard, we are very unique. There are so many great scientists around that you can interact with in person.

The idea of creating a habitat for life sciences research and industry came with the city's donation of 120 hectares of land to General Atomics in 1955 (Veltman, 2003). The city needed new industries which would complement the loss of defense related industries after World War II. The city noticed that the General Atomics research facility grow to be an anchor of high paying jobs without many negative impacts on the natural environment. In 1958, the Regents of the University of California asked the city to prepare a master plan of land use which would adequately support a new university campus. The city wanted to develop the area that could be an important asset to the city as a hub of industries and culture. The master plan anticipated that "as the University grows and matures, it will supplement and become inbred with other great, private enterprise industrial and research institutions… The University should act as a magnet, as well as the aforementioned nuclei for industries presently in San Diego, in attracting more and more of these high level concerns to this area" (City of San Diego, 1959, p. 12-13). Responding to the request, the city submitted a new land use plan titled 'Master Plan for University of California Community' in 1959. In the planning document, the city intended to ensure some portion of the neighboring area should be compatible with research and development activities:

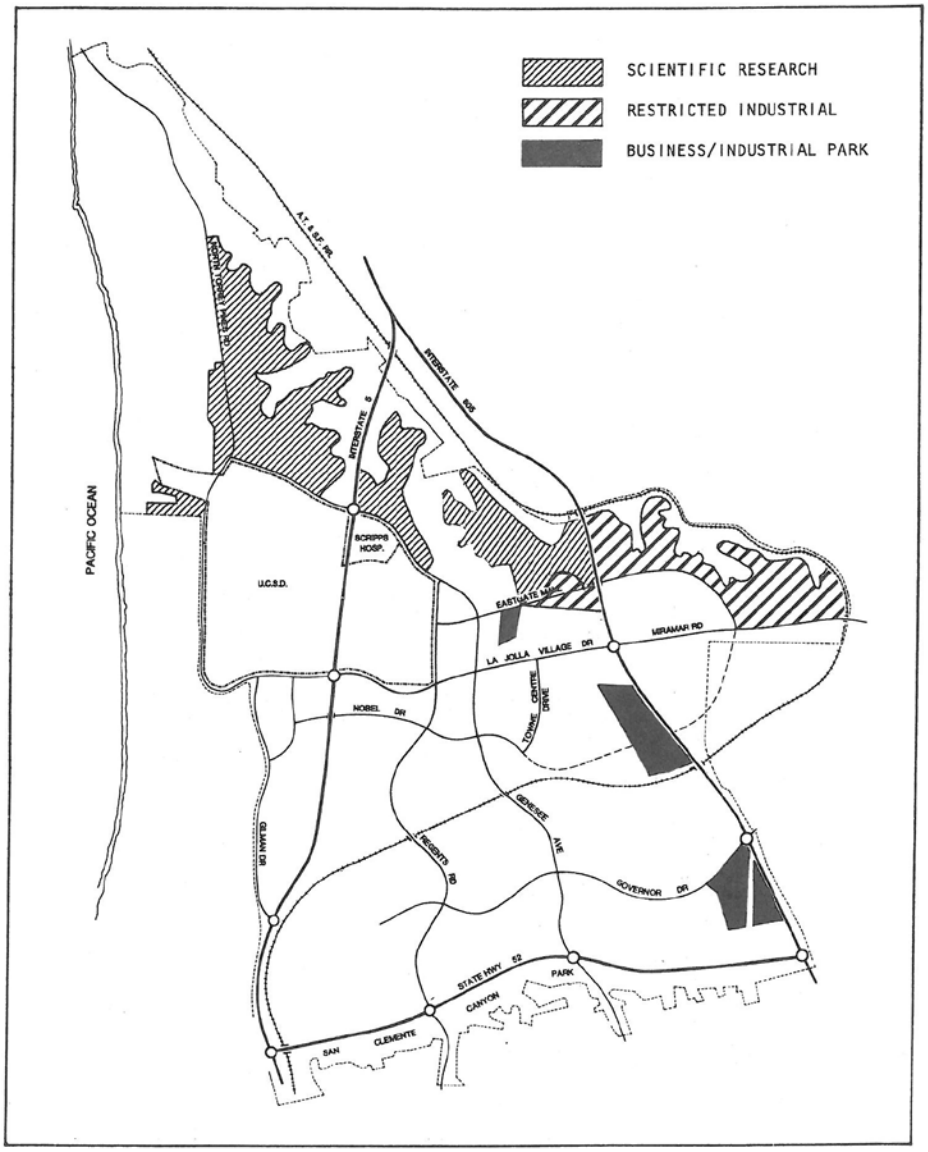
> The developers of this valley area which is now under a single control have been working closely with the University Master Plan developments and are planning on encouraging the use of their land for research and development activities that can tie into and be oriented to the University, similar to Stanford Research Park development at Palo Alto. Deed restrictions are being prepared to augment light industrial zoning now available in the City ordinances, to better insure compatible developments. (City of San Diego, 1959, p. 33)

The city foresaw the university growing up and research facilities emerging in Torrey Pines Mesa. They became more assured of the potential of the area, so they started to specify and reinforce the guidelines in the following decades. In a 1971 plan, zoning ordinances were incorporated. Several parcels of lands around UCSD were designated as part of 'Life Sciences-Research' zone. It stated "the University, together with present complementary scientific facilities and the ever present potential of attracting related establishments, can develop into one of the greatest academic and biomedical health science centers in the country, if not the world" (City of San Diego, 1971, p. 20). The city recognized the significance of high-quality amenities to attract talent and resources to San Diego:

> Equally important to the creation of such a center is the area's magnificent setting and the necessity to provide a quality living environment to attract the scientist and his family to the Community. It is imperative that the best in living, educational, cultural and recreational facilities be provided in the community to assist life science facilities in attracting the best scientific personnel available. (City of San Diego, 1971, p. 20)

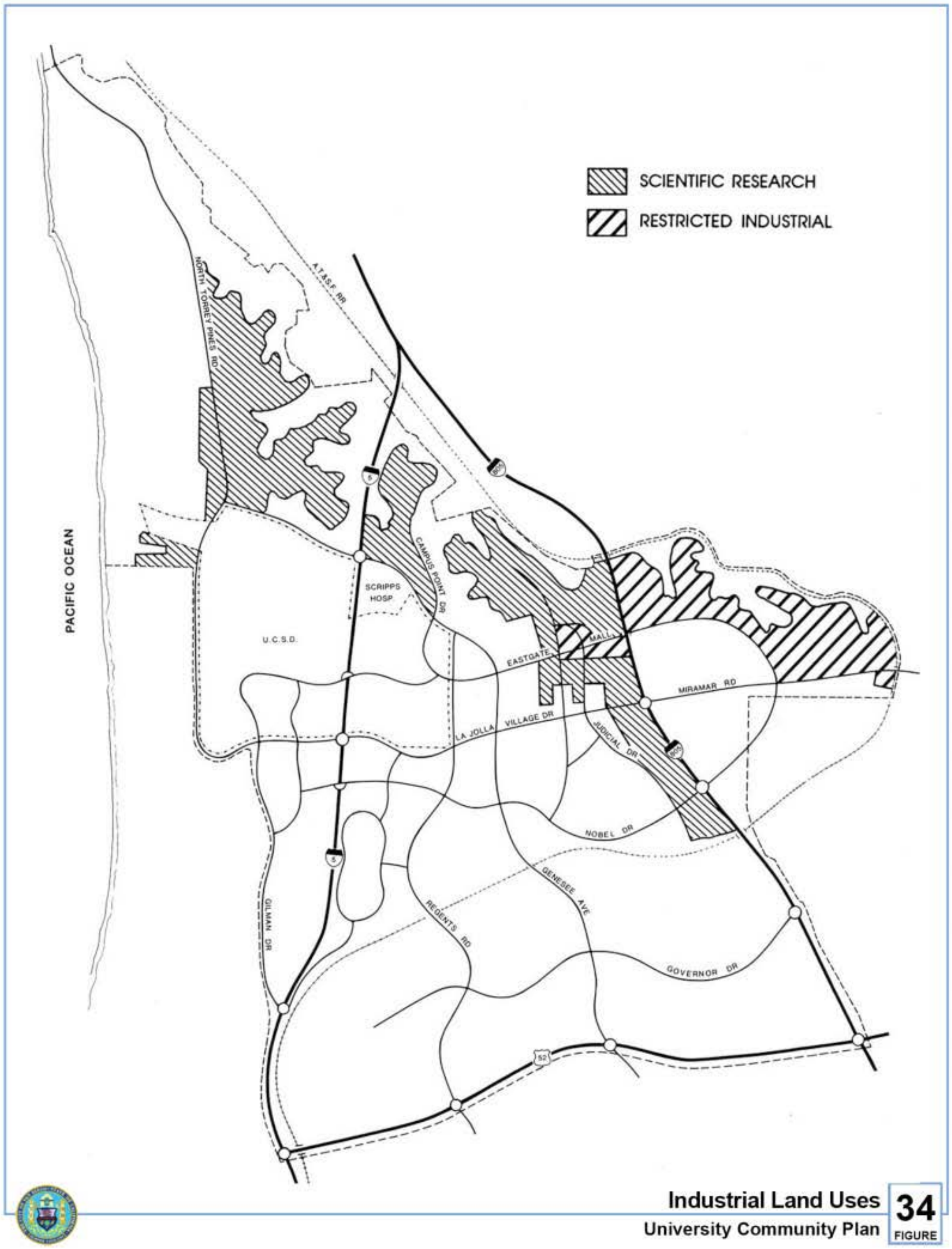
The basic idea of the Life Sciences-Research zone was to create a campus like environment, which would be attractive to talent and enterprises. One of the concerns ever since has been to keep the integrity and intention of the 1959 and 1971 plans of nurturing a scientific and industrial center. In particular, the city and the biotechnology community have been concerned about residential and commercial encroachment. To prevent the encroachment and to reflect the demands of the biotechnology community, the city revised and updated the plan in 1983, 1987 and 1990. In the 1983 plan, the title of the Scientific and Research Zone and a separate section for 'industrial element' were introduced. The Scientific and Research Zone is shown in Figure 4-3, and most of the zone still appears the same in the current planning document (as shown in Figure 4-4). Most non-profit research institutions, including the Salk Institute, TSRI, the Sanford-Burnham Institute, pharmaceutical companies' research facilities and large number of biotechnology companies are located in the zone. The 1983 plan specified the permissible facilities in the zone: "The uses contemplated within the Scientific-Research (SR) Zone are research laboratories, supporting facilities, headquarters or administrative offices and personnel accommodations, and related manufacturing activities" (City of San Diego, 1983, p. 81)

**Figure 4-3.** Scientific and Research Zone in the 1983 plan




*Source*: City of San Diego, 1983, p. 83.

**Figure 4-4.** Scientific and Research Zone in the 1987 plan




*Source*: City of San Diego, 1987, p. 212.

In this plan, the city suggested four goals of industrial development:

- Insure that industrial land needs as required for a balanced economy and balanced land use are met consistent with environmental considerations.

- Protect a reserve of manufacturing land from encroachment by nonmanufacturing uses.
- Develop and maintain procedures to allow employment growth in the manufacturing sector.
- Encourage the development of industrial land uses that are compatible with adjacent nonindustrial uses and match the skills of the local labor forces. (p. 82)

In this plan, the city proposed that "In order to maintain the present quality and cohesiveness of existing science-research parks, the development designs and proposed land uses should be carefully reviewed in these areas" (p. 84).

Each development project in the Scientific and Research Zone must go through a review process whereby the city examines the quality and cohesiveness of the proposal. Through this process, the city has implemented the principles and standards of the plans not just for land uses, but also densities, heights, building designs, building materials and landscaping. A city official (Gibbon, interview) described the regulatory process and the principles:

> Whether the city developed itself or sold to private developers who completed the development process, they created fairly strict development and design standards for each industrial park. As opposed to traditional industrial parks which might be a large flat area of concrete and streets without trees or plants, they wanted to create very high-end industrial parks where people feel almost like a college campus.

He explained that the cluster would not have been possible without the city's land use planning. La Jolla, he said, would be like 'Century City or Santa Monica' which is filled with commercial buildings like office buildings, shopping centers and high-end houses. According to him, the main concept and intention of the planning was to "develop in a way that takes advantage of the university" even though it would take a long time to realize the vision (interview). And "by preserving and setting this idea" for at least two decades, the city began to reap the fruit beginning in the 1980s, as Gibbon (interview) explained:

> It's not an accident. It's because we knew we had this, we got this land. We don't want anything else here. It got to be biotech and scientific research because this is focused on chemistry and biology.

On the Mesa, which had been an abandoned military base, several research and educational institutions arose following UCSD and the Salk Institute. In the Scientific and Research Zone, real estate developers constructed commercial laboratory spaces tailored to the needs of small biotechnology or large pharmaceutical companies. An aerial view of UCSD and the Scientific and Research Zone in Figure 4-5 shows the current topography of research and commercial activity at Torrey Pines.

**Figure 4-5.** Aerial view of research institutions on Torrey Pines Mesa


*Source*: Aerial photo by the Google Maps on http://maps.google.com. Retrieved on October 18, 2010.

### 4-5. Genesis of the Biotechnology Industry in San Diego

Although the city envisioned a future of a biomedical industry, and UCSD and research institutions were expanding on Torrey Pines Mesa during the 1960s and 1970s, the region had to wait a few more decades to see biotechnology companies spawn there. In fact, the biotechnology industry did not exist until the late 1970s. The discoveries of biological processes and mechanisms at a molecular level, and the technology of combining segments of DNA to produce proteins, provided a platform to form a novel industry (Chandler, 2005). The discovery of the double helix structure of DNA by James Watson and Francis Crick in 1953 led to revolutions in molecular biology and genetic engineering in the 1970s. Harvard provided the first course in molecular biology in 1965 and created the first department in 1967 (Chandler, 2005, p. 182). Most major research universities formed departments of molecular biology by the late 1960s. The early evolution of knowledge and practices in molecular biology was started and extended by academic scientists: Stanley Cohen of Stanford University and Herbert Boyer of University of California at San Francisco invented recombinant DNA (rDNA) techniques in 1973; in 1975, Georges Köhler and Cesar Milstein published a paper about a technique of producing monoclonal antibodies (Mabs).

First of all, venture capitalists and academic scientists jumped at the chance to capture the novel knowledge and techniques like rDNA and monoclonal antibodies. Lot of start-ups emerged through the partnerships between academics and investors. Robert Swanson, partner of Kleiner & Perkins (it was renamed Kleiner, Perkins, Caufield & Byers later), a venture capital firm in Silicon Valley, and Herbert Boyer, co-inventor of rDNA technique, founded Genentech in 1976. As the first biotechnology company, Genentech went to the public stock market in 1980 and developed the first genetically engineered therapeutic human insulin in 1982 in collaboration with Eli Lilly. On the East Coast, Walter Gilbert of Harvard University and Phillip Sharp of the Massachusetts Institute of Technology founded Biogen in 1978. It was 1980 when a group of venture capitalists and scientists from universities in California launched Amgen, which has grown to be the largest independent biotechnology company to date (Binder, 2008).

In San Diego, in 1978, Hybritech was founded as the first biotechnology company by Ivor Royston, assistance professor at UCSD, and Howard Birndorf, research technician at UCSD, with funding from Kleiner & Perkins. Prior to the establishment of Hybritech, a growth hormone producer, Calbiochem, was on Torrey Pines Mesa from 1971 to 1977 (Mitton, 1990). However, Hybritech and its managers, who are also referred to as 'fathers' of the community, were the foundation for what was to become the local biotechnology cluster.  is now generally regarded as the origin of the biotechnology industry in San Diego, and its executives are referred to as 'fathers' of the community.

The trajectory of establishing and running Hybritech from 1978 to the 1980s reflects well the local environment for entrepreneurial activity. Royston and Birndorf, founders of Hybritech, came to know monoclonal antibodies, a technique developed by Georges Köhler and Cesar Milstein, when they were working together at a lab of Stanford University (Robbins-Roth, 2000, Ch. 5). As soon as Royston found research on monoclonal antibodies, he became interested in the technique and decided to develop cancer therapeutics from it:

> I thought this could lead to entirely new approach to generating highly specific and high selective antibodies for treating cancer. I was going to be an oncologist, I wanted to develop new ways of treating cancer (Royston, 2006).

In 1977, Royston joined UCSD as an assistant professor, and brought Birndorf to his new laboratory. Within six months, they succeeded in producing monoclonal antibodies. They soon recognized the commercial potential of this research, and started seeking ways of commercializing it.

However, they found it challenging to establish a biotechnology company in San Diego. Lacking knowledge on business and networks, they bought a book, titled *How to Start Your Own Business*, and contacted a few pharmaceutical companies (Sterngold, 1996;

Hardie, 1989c). As they draw attention from Brook Byers, partner of Kleiner & Perkins, and succeeded in attracting an investment of $300,000 from the venture capital firm, Birndorf left UCSD to be the first employee of Hybritech in 1978. Royston stayed at UCSD and participated in the company as a scientific consultant. In the following years, Byers and executives of Hybritech brought in managing and scientific talent as the company grew. They succeeded in persuading Howard Greene, former director of international marketing for Baxter Travenol Laboratories Inc. of Chicago, to be CEO of Hybritech. Greene redefined the business plan, and recruited talent around the country. Many of them were attracted by the opportunities of participating in growing a start-up and in developing monoclonal antibodies technology. During the early 1980s, Hybritech grew up rapidly by succeeding in developing a variety of diagnostic tools based on monoclonal antibodies: the first diagnostics for prostate cancer with the monoclonal antibody technology was one of these products. It went public in 1981, and by 1984, it manufactured fifteen out of forty monoclonal antibody products in the market (Berger, 1984c).

As the Hybritech story shows, the founders and managers of the company had to draw on outside for recruiting talent and acquiring resources. San Diego had no pharmaceutical companies or venture capital firms, which invested in the early-stage biotechnology companies during this time. Indeed, it was not one of the emerging centers for the biotechnology industry. The two founders of Hybritech had to draw on the Silicon Valley in many ways: their entrepreneurship had roots in their experience in Silicon Valley; it was a Silicon Valley venture capital firm, which recognized the potential of technology and invested in them; Byers, a Silicon Valley venture capitalist, brought in the first CEO; many senior managers and scientists came from outside San Diego. Furthermore, faculty of UCSD were not familiar with or supportive of entrepreneurism at this time, therefore, Royston came across confrontations with his UCSD cohort. As an episode, there was a secret faculty meeting at Royston's department to discuss his engagement with Hybritech. Royston (2006) explained how he was mentally supported by Byers: "Don't worry Ivor. We have been through with Cohen and Boyer in San Francisco. You are a pioneer. Arrows always shot pioneers."

Until the 1990s, San Diego lacked any significant base of pharmaceutical, financial or high-technology industries, compared to major cities of the U.S. Indeed, the region lacked the depth and breadth of talent and expertise to establish and run many biotechnology companies. Skills and practices were not sufficiently developed nor imported to commercialize scientific advances at research institutions in San Diego. An analyst of high technology industries pointed to the lack of management talent as one of the most serious barriers to nurturing the local high technology sector:

> I have seen good products in companies that had no business plan, VCs [venture capitalists] like to see a financial manager, a marketing manager, and a strong CEO on the team. If a company is run by the creators of the technology, no matter how good that technology is, the VCs get nervous. (Robert Weaver, quoted in Berger, 1985b)

Up until 1986 when Hybritech was acquired by Eli Lilly, only a few firms sporadically emerged in San Diego each year although science of molecular biology was rapidly expanding and potential seemed unlimited. From the early 1980s, scientists, mostly from UCSD and the Scripps Clinic and Research Foundation, began to establish start-ups to commercialize their scientific discoveries. But, most of these early activities were limited to developing diagnostics or veterinary treatments. During 1981 and 1982, scientists from the Scripps Clinic and Research Foundation founded four biotechnology firms: Syntro, Quidel, Synbiotics and Cytotech. Immunetech Pharmaceuticals was one of a few biotechnology companies, which focused on developing human treatments, not diagnostics or veterinary treatments (Mitton, 1990). Another notable trend during the early 1980s was the creation of spin-off companies by Hybritech and its managers. In 1983, Birndorf and Thomas Adams, senior manager of Hybritech, founded a start-up, Gen-Probe, in conjunction with an independent scientist. Hybritech provided a $2 million equity fund to the start-up (Hardie, 1989a). By 1985, Birndorf formed another company, IDEC Pharmaceuticals, with Royston and a scientist at UCSD to develop cancer drugs. Later, Gen-Probe and IDEC Pharmaceuticals became the most successful biotechnology companies in San Diego: Gen-Probe was sold to a Japanese company at $100 million in 1989 (Perry, 1989c); IDEC Pharmaceuticals succeeded in developing the first cancer therapeutic from monoclonal antibodies – Rituxan, a lymphoma drug, which received the FDA approval in 1997 (Crabtree, 2001).

During this period, another important force was the efforts by research institutions to capitalize on their research capacity. The Salk Institute established a commercial arm, the Salk Institute Biotechnology and Industrial Associates (SIBIA) in 1981. The intention was to leverage the research capacity of Salk Institute to bring in research funding and to provide windows of technological opportunities to its scientists. In the early years, SIBIA did mostly contract research for large companies (Fikes, 1993b). Agouron Institute, founded by UCSD scientists in 1978 as a non-profit research institution, formed Agouron Pharmaceuticals in 1984. This company had the exclusive rights of commercializing research discoveries at Agouron Institute. Agouron Pharmaceuticals focused on developing a technology platform of three-dimensional drug design, named 'structure-based design technology' or 'a rational drug design'. It started an AIDS treatment program supported by a five-year NIH Small Business Innovative Research (SBIR) grant from 1984. By 1997, Agouron became the first local biotechnology company with a human therapeutic drug of Viracept, which was one of the revolutionary drugs treating AIDS (Rose, 1996a; 1997). The La Jolla Cancer Research Foundation, which would be renamed the Sanford-Burnham Institute, established a biotechnology company, Telios Pharmaceuticals, as a subsidy.

The acquisition of Hybritech by Eli Lilly and the creation of CONNECT provided a major boost to the local biotechnology industry. An analysis done by Casper (2007) demonstrates the acceleration of start-up activity from the year of 1986 when Hybritech was acquired and CONNECT was embarked on. In 1986, Hybritech was merged by Eli Lilly at a price of $480 million. Eli Lilly wanted to capitalize on Hybritech's competency with monoclonal antibodies technology to develop a line of therapeutics. People at Hybritech hoped to leverage the large pharmaceutical company's financial resources to develop cancer treatments. Hybritech's chief financial officer, Timothy Wollaeger, explained the need of strong sponsor to pursue its long-term vision: "We looked at our capital needs over the next five to ten years in order to get cancer therapeutics and imaging products into the marketplace and they are considerable" (Kinsman, 1985). At that point, its first therapeutic treating liver tumors was under clinical tests at Johns Hopkins University. In addition, the team of senior managers at Hybritech expected that Eli Lilly would let them operate the merged company on their own.

Soon after the acquisition, many managers and senior-level scientists left Hybritech to either found start-ups or join fledgling companies. Unfortunately, they found themselves uncomfortable in a large pharmaceutical company. Recognizing other opportunities around them, the senior managers started to leave Eli Lilly and join with scientists either from local or outside research institutions. David Hale joined Gensia Pharmaceuticals in 1987, which had been founded by two UCSD researchers in the previous year. Along with ups and downs, the company has spawned three biotechnology companies, while it has transformed itself to be a specialty pharmaceutical company. Howard Greene and Timothy Wollaeger founded a venture capital firm, Biovest Partners, which was instrumental in establishing several start-ups. Dennis Carlo joined with a group of scientists from the Salk Institute including its founder, Jonas Salk, to form Immune Response, an AIDS vaccine developer. Cam Garner turned a staggering biotechnology firm into a nursery of a series of specialty pharmaceutical companies. Royston participated in building up a non-profit research institution, the Sidney Kimmel Cancer Center, which focused on developing cancer therapeutics and then established a local venture capital firm, Forward Ventures. Birndorf continued to be involved in forming a number of biotechnology start-ups.

After the acquisition of Hybritech, start-up activity became much more vibrant as virtually every senior manager left to launch their own ventures or joined at fledging ventures. At the same time, the Hybritech people became the engine of communal efforts to nurture entrepreneurship. They were involved in establishing CONNECT and formed a core group of mentors or advisers, who helped many academic scientists launch businesses.

Besides the spin-offs by Hybritech alumni, many scientists and entrepreneurs launched biotechnology start-ups. Promising technologies were continually coming out from the local and non-local research institutions. Throughout the 1980s and 1990s, the expectation and excitement on biotechnology were high enough to draw continuous investments from the public and the pharmaceutical companies. Venture capital firms began to set up local offices or strengthened affiliations with the local biotechnology community from the late 1990s. Gradually, San Diego emerged as a technological center of gene therapy, gene analysis and X-ray crystallography.

Pharmaceutical companies started to build their research facilities in La Jolla to tap into the local talent and scientific expertise from the late 1990s. The coming of large pharmaceutical companies to San Diego was not accidental. They came to San Diego after several years of collaborations with local biotechnology companies, research institutions, and their series of acquisitions of local start-up companies. The previous experience of collaborations, for example, led Novartis to build two R&D facilities, Genomics Institute and Novartis Agricultural Discovery Institute. Pfizer established a research facility by merging Agouron Pharmaceuticals – developer of an AIDS drug, Viracept – to be more specific, Pfizer acquired Warner-Lambart, which had bought Agouron Pharmaceuticals. The influx of large pharmaceutical companies both promoted the area's prominence and brought in a caliber of seasoned executives.

**Table 4-3.** Venture capital investments in the biotech industry in San Diego, 1995-2009

($ millions)

| Year | U.S. | San Diego | S.D. % of U.S. |
|---|---|---|---|
| 1995 | 748 | 67 | 9.0 |
| 1996 | 1,135 | 128 | 11.3 |
| 1997 | 1,319 | 142 | 10.8 |
| 1998 | 1,492 | 169 | 11.3 |
| 1999 | 1,995 | 225 | 11.3 |
| 2000 | 3,975 | 574 | 14.4 |
| 2001 | 3,321 | 569 | 17.1 |
| 2002 | 3,194 | 455 | 14.2 |
| 2003 | 3,607 | 353 | 9.8 |
| 2004 | 4,217 | 582 | 13.8 |
| 2005 | 3,973 | 591 | 14.9 |
| 2006 | 4,598 | 560 | 12.2 |
| 2007 | 5,266 | 957 | 18.2 |
| 2008 | 4,349 | 421 | 9.7 |
| 2009 | 3,533 | 445 | 12.6 |

*Data Source:* PricewaterhouseCoopers & National Venture Capital Association. Money Tree Report. Retrieved from https://www.pwcmoneytree.com/MTPublic/ns/index.jsp. Retrieved on June 21, 2010.

Combined with the newly growing tradition of entrepreneurship, the local community continues to expand and diversify its learning and interacting base. In the late 1990s, a group of angel investors and retired entrepreneurs organized a network for angel investing. The School of Engineering at UCSD launched a center, the von Liebig Center, to help faculty and students initiate entrepreneurial activity. A UCSD student organization and the angel network started business competitions, respectively. San Diego began to rise as one of the most vibrant biotechnology hubs. The County of San Diego accounted for about 13 percent of the nation's venture investments from 1995 to 2009 (Table 4-3). In addition, Table 4-3 shows the rising trend of the venture investments in local biotechnology companies.

**4-6. Coming of a New Perspective**

Until the mid-1980s, the local governments and San Diego Economic Development Corporation (SDEDC) focused on attracting large companies and research consortiums, and they paid attention to expanding the military base. To achieve this goal, local governments and trade associations led their efforts by advertising and marketing San Diego. San Diego was 'a branch office town' without any substantial tradition of, or resources, for a self-sustaining economy. San Diego, as a journalist wrote, was "in a sense a third-world colony of the big financial and corporate interests with their home base elsewhere in California, in other parts of the United States, or abroad" (Fredman, 1984a). Therefore, the emerging biotechnology and high-technology start-ups had to attract talent and capital from outside San Diego.

Traveling to and observing what was happening in Silicon Valley, individuals in San Diego started to acknowledge the potential and possibility of nurturing high technology and biotechnology industries locally. Silicon Valley had already emerged as the national center of innovation and entrepreneurship. Civil and business leaders in San Diego began to understand that the community should build up leadership and partnerships to nurture start-ups. An address by an entrepreneur in information technology industry is illustrative of the appreciation: "If we are to create Silicon Beach, we have to generate a community commitment backed by the technology and the educational base that already exists here" (Peter J. Shaw, quoted in Berger, 1984a).

Along with the new recognition, failures to attract two research in 1984 and 1985 were critical to turning attention to nurturing start-ups, instead of attracting established companies from outside. Recognizing the potential for attracting outside companies, the civil and business community initiated communal endeavors to locate two industry consortiums in 1984 and 1985. In 1984, the San Diego Economic Development Corporation (SDEDC) led a communal effort to attract the Software Productivity Consortium (SPC). This was a joint venture of thirteen aerospace companies to boost computer technologies by combining their capacity and resources. SDEDC and the region thought that the consortium could be an anchor drawing the participant companies to San Diego as well as a nursery for spinning off start-ups. Daniel Pegg, president of SDEDC, explained the motivation of the community: "We're getting close to that critical mass where the technology tends to be self-generating – where the university spins off little companies" (Berger, 1984d). San Diego sought to capitalize on its research institutions. Unfortunately, the consortium went to Virginia (Coleman, 1985).

Undeterred, SDEDC set their sights on another consortium. In the following year, SDEDC with the support of the city government and UCSD embarked on another initiative to lure the Microelectronics and Computer Consortium (MCC) to San Diego. SDEDC formed an advisory group, including Richard Atkinson, Chancellor of UCSD, and leaders in the business sector to combine the non-profit and for-profit sectors. Although San Diego succeeded in being one of the four finalists, this consortium also went elsewhere. It went to Austin because of the Texas state government's pledge to build world-class R&D capacity at the University of Texas (Castro, 1985b). By experiencing the consecutive failures, the local people learned two lessons: they realized the importance of partnership between academia and industries, and the role of a research university in promoting technology-based industries. Daniel Pegg noted, "the lesson that the community learned from losing the MCC was that it had to pull together" (Innovation Associates Inc., 2000, p. 40). Similarly, David Hale, president of Hybritech, commented: "The community has realized that for San Diego to attract high-tech companies there needs to be a concerted effort among industry, academic and business interests" (Castro, 1985a).

In another setback, SDEDC failed to bring in any established companies to San Diego in 1984. The region was concerned with the outflow of manufacturing companies to offshore and its effect on the local employment. The region sought to fill in the decling employment base by attracting established companies from outside. In attracting established firms, the region emphasized its growing research base, geographical location on the Pacific Rim and its sunshine (Castro, 1984; Coleman, 1984; Fredman, 1984b). But the mission turned out to be difficult to accomplish as its living costs were rising, and the competition between regions was becoming more robust. Daniel Pegg explained: "they don't locate here for various reasons. These include possible water shortages, the cost of housing and utilities, etc." (Lowe, 1985). He continued "The competition is also looking at San Diego and saying, 'we want that'. They're becoming more competitive by building up their academic base and infrastructure too. Almost every week a raider from other states comes here trying to lure our business away" (Lowe, 1985).

In 1985, SDEDC embarked on another initiative. Joining with local businesses and governments, SDEDC put a special advertisement in the Forbes magazine. In the advertisement section, the local community tried to present its opportunities to outside companies. The special advertisement ended as: "Across the board, San Diego's business climate is perfect. And the weather's not bad, either" (SDEDC, 1985). But these efforts did not turn out fruitful in the following years, and during the early 1990s, SDEDC encountered harsh criticism for wasting city budget (Coburn, 1990; Navarro, 1992; Deerlin, 1992).

SDEDC and the local business community commenced an endeavor to attract another research consortium, the Semiconductor Manufacturing Technology in 1987. But they discontinued the effort soon after submitting a proposal. Daniel Pegg commented: "It's [proposal] essentially been rejected because of its lack of incentives… I would much rather have a solid corporate citizen, a TRW, a Rohr, a couple of biomedical companies"(Perry, 1987). During the last a few years, the community had started to recognize the importance of home-grown high technology and biotechnology companies, as indicated in David Hale's account: "There is a recognition that if San Diego is going to continue to grow in terms of jobs, then the growth will come from businesses that are started and built here" (Perry, 1987).

After SDEDC gave up the bidding, it sent letters to local firms reassuring the support and commitment from regional institutions including SDEDC itself. This action was accepted as an important step toward focusing on home-grown start-ups. A journalist greeted this effort as a meaningful step in shifting resources and efforts to supporting local companies rather than to luring large businesses from outside:

> This region long has neglected concrete aid to tiny local businesses… Millions of dollars have been spent in largely fruitless efforts to persuade giant businesses to relocate here. Few genuine heavy-hitters have done so… While we pursue the mirage of big employers coming here, the gold in our own backyard – in job creation, diversification and entry into important high-tech areas – is neglected. (Fredman, 1987)

After more than two decades, Mary Walshok (Eger & Walshok, 2008) recalled the new platform that the community began to enact:

> I think what we understood in San Diego 25 years ago, a lot of other communities are only now beginning to understand is that you can build a robust economy on small companies. You don't just have to have big companies and that knowledge is what's gonna drive new forms of economic development… What San Diego did was it realized the future was in the small companies, and it realized that you had to link all these wonderful researchers from the military, the university and elsewhere with entrepreneurs and investors. And we created a new economy.

Through these experiences, business, academia and public leaders reached a consensus that they could build a prosperous economy by nurturing a mass of small biotechnology and high technology companies. They turned their attention and resources to enabling and encouraging entrepreneurs and scientists to create start-ups.

**4-7. CONNECT, the Organizer of Community**

In 1985, a series of communal efforts were embarked upon to support small high technology and biotechnology companies. First, a group of service providers in partnership with SDEDC and UCSD started an investment liaison program – the San Diego High Technology Financial Forum – to help local companies link with investors mostly from outside. Through this annual event, technology-based companies presented their business plan to a group of invited investors, including venture capitalists, institutional investors and angel investors. Second, the MIT Alumni Association of San Diego launched the MIT Enterprise Forum, where panelists of seasoned entrepreneurs provided advice to start-up entrepreneurs. Third, and most importantly, an incubating program, CONNECT, was started.

CONNECT was conceived and constructed as a consequence of engagements and experience during the failed efforts to locate research consortiums. Richard Atkinson, chancellor of UCSD, was involved in the series of failed efforts to attract research consortiums in 1984, 1985 and 1987. Especially, during a series of discussions to locate MCC, the participants recognized that the university and industry were separated from each other. Daniel Pegg (interview) said of the recognition:

> Out of that competition for MCC, came recognition that we really didn't have the connection to our university resources. We needed to bridge between the private sector and the university. The concept was to help bring the university leadership,

> internal talent and the scientific resource together with their counterparts in the private sector.

Atkinson was actively participating in community events and meetings with business people. He sought to leverage the research capacity of UCSD in nurturing entrepreneurial activity. UCSD had grown into a powerhouse of academic research, but it had been insulated from the main part of local economic activity. The scientists and UCSD itself were neither familiar nor comfortable with entrepreneurial activity.

Amid the failures to locate research consortiums and attract established large companies, Daniel Pegg did research on how to capitalize on research universities. Based on his research on academia-industry partnership, he discussed with Atkinson how to connect the university with the local industry. Pegg (interview) said of the initial discussion with Atkinson: "we sat down with and discussed with Dick Atkinson, who was very open and receptive to the idea." Atkinson organized a group by asking "some of his key staff to explore a proper route for the university to assist in reinvigorating the regional economy" (Walshok, Furtek, Lee, & Windham, 2002, p. 36). The group held a series of discussions to find ways to facilitate the interactions between UCSD and industries. Pegg (interview) recounted the process of initiating a new program:

> We got together, and discussed different possibilities and different ways to approach the issue and to finance. It just grew from there. Then, shortly after, we had an initial concept, and it was, in great part, the work of Mary Walshok and those who originally sat around the table and discussed the issue.

During his tenure of 25 years at Stanford, Atkinson observed how Frederick Terman, provost of Stanford University, who is regarded as the creator of Silicon Valley, was transforming Stanford University and Silicon Valley. During his directorship of the

National Science Foundation (NSF) from 1975 to 1980, he led an institutional effort to reinvigorate cooperation between academia and industry. Atkinson (interview) recalled, "by 1975 when I went to the NSF, there was a real concern about the whole evolution of technology and innovation in the United States. That concern was how to facilitate the application of basic research." He set up a research group at the NSF to explore policies and programs to leverage basic research to stimulate entrepreneurship and innovation. He was involved in enacting the Bayl-Dole Act of 1980, which allowed universities to hold title to inventions and to license intellectual property rights exclusively to commercial entities.

Atkinson was well aware of the importance of academia-industry relationships, and he was open to the industry due to his experience at Stanford University and efforts at the NSF. The initiative was to utilize the potential of the relationship between UCSD and local industries. He described the influence of Terman:

> I was able to apply the knowledge I gained from Fred's work at Stanford years later when I became chancellor of the University of California, San Diego (UCSD). I sought to use the "Terman Model" as a roadmap for UCSD's partnerships with the telecommunications and biotechnology industries that were beginning to spring up in the region, and I encouraged the development of UCSD's own peaks of excellence. (Atkinson, 2004, p. ix)

In writing, he described his intention and idea of engaging in the local economic activity:

> I also wanted UCSD to play a very aggressive role in the development of high-tech industry in the San Diego region. The model that I had in mind was rooted in my experiences as a professor at Stanford from 1956 to 1975 and as a director of the National Science Foundation in the late 1970s. (Atkinson, 2008)

The staff began to explore a platform to stimulate engagement of their academic scientists in entrepreneurial activity. They started contacting local business leaders and scientific entrepreneurs like Irwin Jacobs, founder of Linkabit and Qualcomm, and Ivor Royston. According to Walshok et al. (2002, p. 36), "one-on-one interviews and round tables yielded a number of creative ideas about how the university and the community could collaborate on this issue." Walshok (interview) remembered how she and the community had encountered this core idea of a new program in the course:

> Atkinson asked me to go out and interview business leaders and successful entrepreneurs about what they thought would help grow companies locally. I heard two things. When I talked to the business people – lawyers, accountants, some marketing people, real estate people – they said, “you must teach the scientists how to think like businessmen, how to write business plans. They must understand markets, they must understand profits and application.” I also talked to the successful entrepreneurs like Irwin Jacobs and Ivor Royston, and they said, “you must teach the business community about science. They only know how to build shopping centers and real estate developments. They only understand old industrial companies. We need lawyers, accountants, marketing people, real estate developers who understand R&D companies – physics-based, chemist-based and biology-based companies – which are going to be global from day one.”

Out of the 40 people who the staff had contacted, thirty responded. Based on the discussions and 17 company sponsors, a new program was embarked with $75,000 seed funding (Castro, 1985a; Rose, 1989). Irwin Jacobs, founder of Qualcomm and also one of the cofounders of CONNECT, explained why he and the business community participated in (or led efforts of) embarking on a new program:

> At the time, it was a lot harder to start a company here in San Diego. There weren't many people: some defense companies here, but the banks, the lawyers and the accountants weren't used to be here. There was a need for a community of support, a whole eco-structure… It was useful having a community of support. Some folks at UCSD also were thinking along the same line and suggested that we start an organization to do this. So, I certainly supported that and put together CONNECT. (interview)

Walshok (interview) emphasized the importance of the bottom-up approach of the new program: the core ideas and values came from the local people, and the organizers and advisers were mainly composed of scientist entrepreneurs and local businessmen. She (interview) explained: "It wasn't governments, it wasn't professors of business, it wasn't outside experts. It was the local community organizing and taking the advice of these early entrepreneurs who were so successful."

This program was originally named 'Program in Technology and Entrepreneurship', as part of the university's Extended Studies and Public Programs, and later it was renamed CONNECT. The early focus was to integrate the competency of UCSD and local industry by stimulating interactions and interchanges. To the people from industries, UCSD was too bureaucratic and detached from the local economic life. To achieve the goal, the both sides needed an intermediary agent which would bridge the chasm. Walshok (Eger & Walshok, 2008) stated the vision of the program:

> The whole premise of this CONNECT program was that you can turn promising inventions and ideas into viable businesses for which there are markets, where you can make money and create jobs if you can link the research university with the business community and the financial community, and build teams that can take an idea into the commercial market place.

CONNECT intended to facilitate commercialization of technologies coming out of the local research institutions. At the beginning, the participants did not expect that the program would be the incubator of a stream of start-ups and collaborative initiatives. What the business community initially expected with the program was to increase its local visibility. David Hale stated:

> The program is not necessarily going to cause companies to be successful or not be successful. But it will create a good environment for high tech in that it can be a mechanism for establishing an image across the country that San Diego is a good place for high tech. That's going to be very worthwhile to attract new people and benefit those companies already operating here. (Castro, 1985a)

William Otterson joined the program as an executive director in 1986. Prior to joining CONNECT, Otterson had led three high technology firms, and had been involved with UCSD by serving as a co-president of UCSD's Cancer Foundation (Berger, 1986). He had developed solid management knowledge and expertise based on his own business experience. He emphasized that the program should be a stepping stone for first-time entrepreneurs and scientists by linking them with the resources and expertise of seasoned entrepreneurs. Walshok noted how Otterson came to CONNECT and built the program:

> When UCSD launched its innovative program in technology and entrepreneurship, we knew we needed an energetic, successful entrepreneur to create something better than a research park or incubator. We found Bill Otterson. I had to convince him that he wanted to work within a large bureaucratic organization like the University of California…But once we got going Bill developed a new model for cultivating the banks, venture capitalists, law firms, accounting and other support companies needed to launch new scientific ventures. (University of California, San Diego, 1999)

During the early years, Otterson focused on enlisting and encouraging experienced executives to work with start-up entrepreneurs who had not gained solid base of experience. He also led efforts to promote collaborations between research institutions. Duane Roth, current CEO of CONNECT, described it this way:

> As entrepreneurs and start-ups formed, he had them talking to each other and collaborating. He was also very successful in engaging research institutes to collaborate among themselves. (interview)

He participated in early programs like Financial Forum and Corporate Partnership Forum, and gave journeymen's guidelines to start-up entrepreneurs. He began the ‘Bill Otterson Biotech Letter,’ which was faxed weekly to the local business community. The newsletter "was an important part of the community, which made sure everybody knew what was going on and recognized successes" (Abigail Barrow, interview). Entire budget came from the business community, including its sponsors and members, while the involvement of UCSD was limited to its participation in the program's scientific board of advisers (Rose, 1989). The organization began to institutionalize its efforts of linking start-up entrepreneurs with resources and the veteran entrepreneurs. They built a spectrum of platforms, whereby people, competence and specialties would congregate.

Gradually, Otterson and staff introduced new programs. To link the scientific discoveries and experiences of entrepreneurs, CONNECT started two programs, 'Meet the Researchers' and 'Meet the Entrepreneur' in 1986. In the following year, CONNECT launched an award ceremony, the Most Innovative Products Awards (MIP). The ceremony, in words of Barbara Bry, who joined the program at the beginning as an associate director, was to "let people know about the innovations that are taking place" and to "give the inventors some recognition" (Douglass, 1988). Beginning with three categories of biotechnology/biomedical, high-tech electronics and 'other', it has become an important platform where the local community recognizes and celebrates the entrepreneurial endeavors of start-ups. In 1989, in response to a suggestion of David Hale, CONNECT started the San Diego Biotechnology/Biomedical Corporate Partnership Forum (Kupper, 1998b). Selected life sciences companies could present their opportunities to a group of invited potential investors of pharmaceutical companies, investment bankers and venture capitalists. In 1990, CONNECT took charge of the San Diego High Technology Financial Forum, which had been originally started by a group of service providers in 1985.

In 1994, CONNECT launched its flagship program, Springboard Program, as a platform linking a group of veteran entrepreneurs with newcomers. In this program, start-up entrepreneurs give short presentations to a panel of experts, which identified obstacles and opportunities, and provided guidelines. Following the panel presentation, the young entrepreneurs or scientists were connected with seasoned entrepreneurs, who would lead by coaching for six to twelve months (Chambers, 2007). Particularly, this program has helped scientists with technological expertise but lacking experience in business turn into entrepreneurs. They are introduced to the community of entrepreneurs and investors through this program as well as a stock of business knowledge. As an example, a scientist at UCSD came across an interactive molecular modeling technology which he wanted to commercialize. After participating in the Springboard program, he commented on his experience: "I wouldn't be starting this if I had stayed at North Carolina or any other place. CONNECT really helped out and gave me a push forward" (Mark Surles, Quoted in Fikes, 1994b).

Abigail Barrow (interview), who had worked to formalize Springboard, told the key impact of the Springboard program was to create and maintain the network of people:

> What we were doing at the Springboard program with early stage entrepreneurs was getting everybody around the table to help them think through the process

> and talk to each other. The people met each other across the table at the program, and it made sure that they had a very well networked community.

By participating in a line of programs, the novice could become a member of the community in which they would locate themselves and on which they would draw resources.

In addition to the programs, CONNECT and Otterson created a space where industry, academic and public people could interact with each other. Through the programs of CONNECT, the participants learned how to collaborate to achieve mutual goals. The experience and encounters at CONNECT resulted in forming a group of networking and advocating associations. In 1989, a networking group, Athena, for female executives in biotechnology and high technology industries was formed with help from CONNECT. In 1991, a group of CEOs of biotechnology companies and service providers formed a trade association, BIOCOM. Another trade association of software companies, the San Diego Software Industry Council, was set up in 1992 with guidance of Otterson and Daniel Pegg. In the following years, a group of trade associations and a series of communal initiatives emerged in San Diego to deal with each group's specific issues.

Much of CONNECT’s success can be attributable to the extraordinary commitment of Otterson. Otterson was actively engaged in advocating the start-ups community. He worked with local trade groups in their efforts to change the attitudes and routines of the university and the City of San Diego. Most of all, he and his team were dedicated to mobilizing the community. As an example, the CONNECT team, in Otterson's words (Bigelow, 1997), "got on the telephone and made 4,000 telephone calls" to organize an award ceremony, the Most Innovative Product Awards, of 1997. In these early years, social capital had not yet developed solidly, and it was the individuals' commitment and dedication, which bonded the community. David Kabakoff (interview), currently a venture capitalist, described Otterson's leadership:

> He was the real driving force behind this, and put a lot of energy to get people together and really showing the community the path to stimulate entrepreneurship. He was a very influential guy and people had respect. If he asked to help, people responded because he was doing that everyday 24 hours seven days.

Daniel Pegg (interview) also attributed the success of CONNECT to the early leadership of Otterson and its co-founders:

> When Bill Otterson had it working with Mary Walshok and the board, everybody was motivated on the ongoing basis because Bill would energize the leadership to rally around different issues. People weren't anxious to be involved. He created a situation and environment where people wanted to help make that more successful.

By the time of his death in 1999, Otterson had created a "comfortable hub for the technology company people to congregate in." (Peter Preuss, quoted in Bigelow, 1999) David Hale recalled how the community had changed by virtue of his effort:

> He made it a cause celebre to be a supporter of the high-tech industry. When I first got here with Hybritech, there wasn't anybody around who cared about biotech or knew about anything about it… Back when biotech was nothing, Bill was able to get the lawyers and the accountants and the other support people to get behind us. (Bigelow, 1999)

### 4-8. Growth of Biotechnology Industry in San Diego

CONNECT and Otterson created a space, where biotechnology and high technology entrepreneurs interacted and collaborated, but still it was through collaborative efforts to over an economic crisis during the early 1990s when these technology-based industries formed partnerships with local governments and were recognized as a main source of economic development. Until the 1990s, biotechnology entrepreneurs had to overcome concerns and confronts by local governments and the public. After several years of R&D activity, many biotechnology companies needed manufacturing facilities and expanded research laboratories by the early 1990s. In pursuing permits, they encountered conflict with the local government. A developer, James McGraw, noted the concerns of the biotechnology companies:

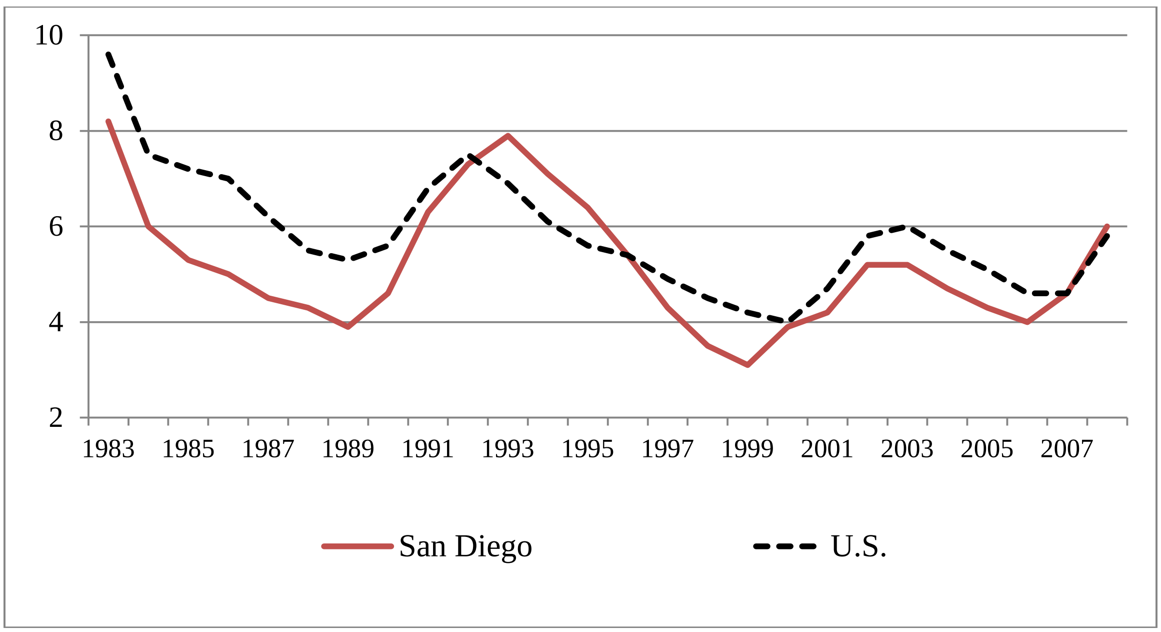
> For example, there's a lack of predictable timing in the planning and development process. There are a number of hoops you have to jump through ranging from community group review of the proposed facility to last-minute environmental concerns. Time is critical for these guys because they have commitments to their investors to come on line. (Quoted in Fikes, 1991a)

Similarly, David Hale commented: "Much of the frustration is the perceived attitude of the City Council and city government in terms of support of this industry. I think attitude is a key issue." (Fikes, 1991b) To be worse, in 1991 the city introduced a water-rationing program, which would discontinue water supply for a few hours every day to industries. Moreover, a group of local environmentalists proposed an ordinance, the 'Toxic Free Neighborhoods Ordinance' in the same year. According to the ordinance, industries were obliged to report any hazardous materials, which most biotechnology companies had to use (Fikes, 1991c). The biotechnology industry had the most concern over the conflicts and confrontations with their local governments. A biotechnology entrepreneur, Jerry Caulder, complained: "Just penetrating the bureaucracy is difficult (in San Diego), and it's hard to predict what the (requirements) are going to be for everything from water to manufacturing" (Douglass, 1992).

By contrast to the expansion of biotechnology industry, San Diego encountered the worst economic downturn in its modern history. In the process of dealing with the economic recess, the local governments and the region acknowledged the importance of the newly emerging industry, and they developed partnerships and strategies to foster the cluster. Historically, the economic prosperity of San Diego coincided with the increase of military expenditures. The contribution of military spending to the Gross Regional Product (GRP) of San Diego peaked to 22 percent in 1987, with $9.2 billion inflow to contractors and payrolls. But, soon San Diego had to confront a new reality: changes of political and diplomatic relations with the Soviet Union along with the expanding federal budget deficits during the late 1980s and the early 1990s forced the federal government to cut military spending. In 1986, Congress voted to compel the Reagan administration to comply with the SALT 2 treaty, an arms-control treat with the Soviet Union. Faced with the sudden collapse of the Soviet Union in 1991 and the escalating budget deficit, the Bush administration embarked on a five-year plan of reducing 25 percent of defense expenditures (Kreisher, 1992).

The cut-off rippled to the economy of San Diego and California. By 1997, the contribution of defense budget to the local economy went down to 11.6 percent in terms of GRP. Military contractors started to close down or downsize workforce of their manufacturing facilities. General Dynamics alone cut 4,800 local jobs by 1994 (Bigelow, 1995). Unemployment rates in San Diego rose over the national average in 1993 for the first time in the last decades (see Figure 4-6). Still worse, the Southern California's real estate recession of the early 1990s deepened the economic hardship. All the four major local banks either went bankrupt or were sold during this time. According to a survey from the San Diego Association of Governments (SANDAG, 1998), the jobs in defense and transportation manufacturing plummeted by 53 percent during the six year period (see Table 4-4). The number of jobs in the financial services sector went down by 35 percent.

**Figure 4-6.** Unemployment rates of San Diego compared to the U.S.




*Data Source*: Employment Development Department of the California State Government, Labor Market Information Division. Retrieved from http://www.labormarketinfo.edd.ca.gov. San Diego indicates the County of San Diego.

**Table 4-4.** Average annual employment, 1990 and 1996: San Diego regional employment clusters

| | 1990 | 1996 | Changes in Numeric | Changes in Percent |
|---|---|---|---|---|
| Defense & Transportation Manufacturing | 39,114 | 18,571 | (20,543) | (53) |
| Financial Services | 15,750 | 10,257 | (5,493) | (35) |
| Biotechnology & Pharmaceuticals | 11,017 | 21,725 | 10,708 | 97 |
| Communications | 6,890 | 11,433 | 4,543 | 66 |
| Software & Computer Services | 8,804 | 13,643 | 4,839 | 55 |
| Business Services | 48,159 | 61,771 | 13,612 | 28 |

*Note:* Among 15 sectors, the author selected six, which represent the economic transformation occurred during the period of 1990 and 1996.
*Source*: SANDAG, 1998, p. 8.

In response, the City of San Diego constituted a taskforce team, The San Diego Economic Development Task Force, with a group of business people to identify economic issues and recommendations to the City Council (Fikes, 1991b). The recommendations by the team included offering incentives to retain local industries, streamlining regulatory procedures and building infrastructure (Brydolf, 1991). In the following years, the city became involved in a series of programs and initiatives supported by funding from federal agencies to mitigate the military impacts. As one of the regional level initiatives, the San Diego Association of Governments (SANDAG) conducted research to identify the potential of newly emerging industrial clusters. In 1993 and 1998 publications (SANDAG, 1993; 1998), the association endorsed the home-grown businesses, as told by its chief economist:

> The old form of economic development – go out and try to find new jobs to come here – has to give way to retaining business and looking internally. We have all the building blocks for manufacturing in three main areas: biotech-biomed, precision

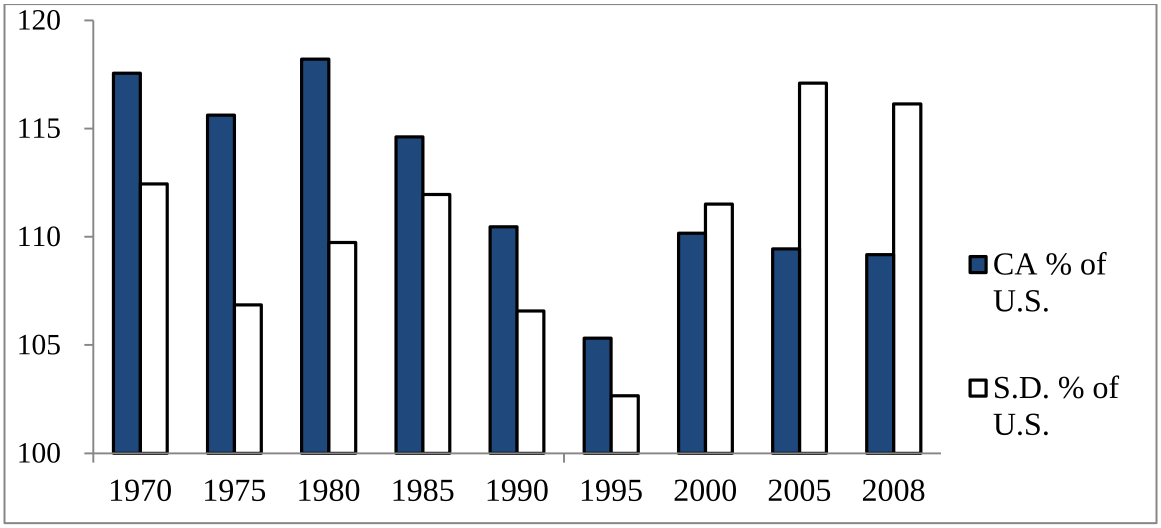
> measurement-medical instruments and telecommunications-fiber optics. (Marney Cox, quoted in Sullivan & Cox, 1993)

In his column in San Diego Union-Tribune in 1996, Daniel Pegg (1996) declared that the region had built its economic base with high-technology industries:

> The great news is that the military is no longer viewed as San Diego's sole employer. San Diego has toiled to create a diversified economy, based not only on the historic standbys of manufacturing, tourism and defense, but on the industries of the future: telecommunications, electronics, software, biotechnology and global trade… And therein lies the success behind San Diego's economic growth and future: San Diego is truly a Mecca for entrepreneurs… There has been a lot of talk lately about the need for Fortune 500s to put down roots in San Diego. Someday, individuals voicing that concern will realize San Diego doesn't need transplanted trees – we're dedicated to growing our own seeds.

It was 1998 when the County of San Diego started to outperform California in terms of personal income for the first time in the modern period (refer to Figure 4-7). As featured in the magazine Forbes, San Diego "is a comeback story of a metropolis rocked by military downsizing at the end of the Cold War" (Ferguson, 1999). The economic conversion occurred because of, to a large extent, the rise of the biotechnology and high technology industries.

**Figure 4-7.** Historical Changes of Per Capita Personal Income Compared to California



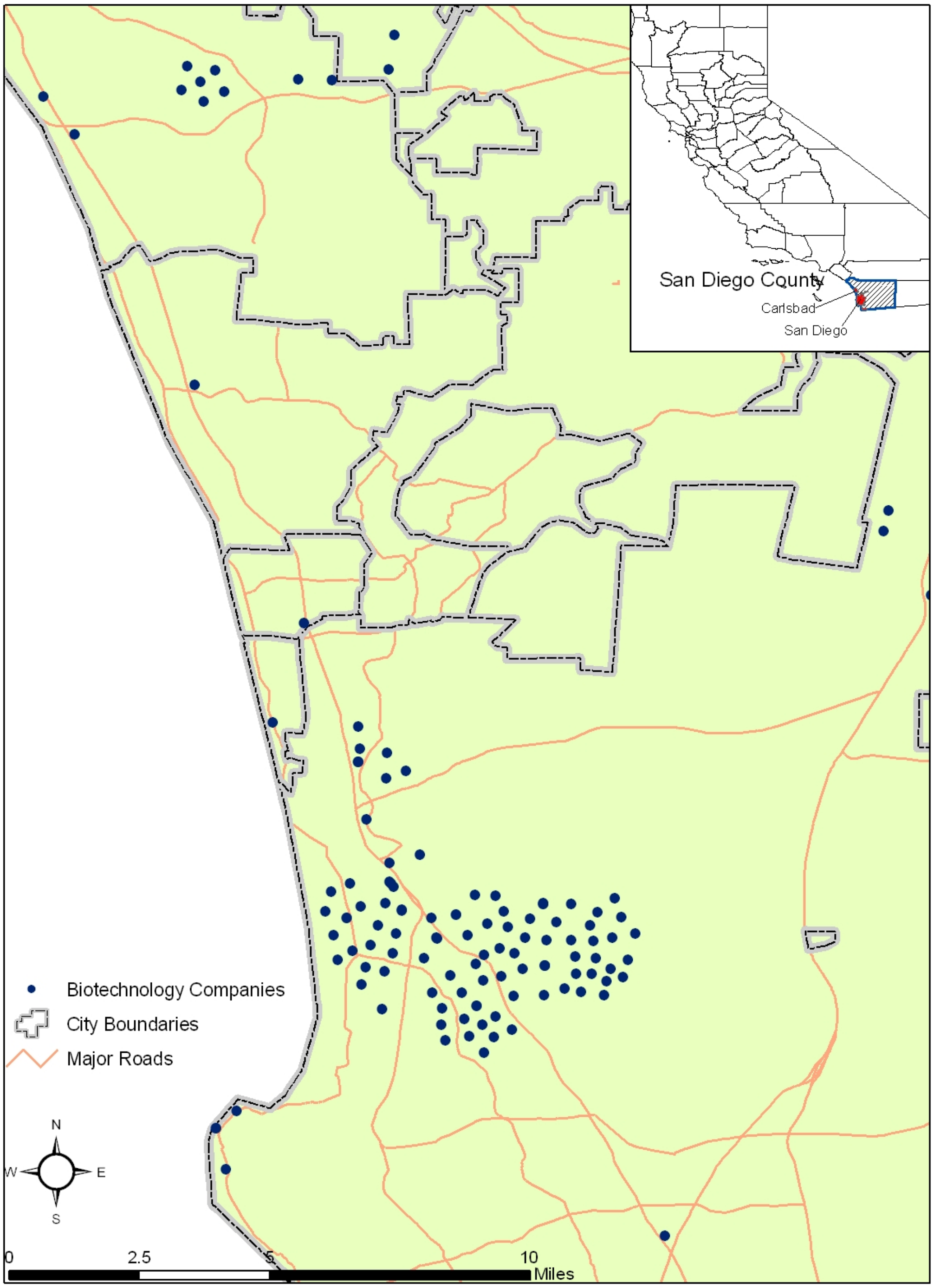

*Note:* San Diego indicates the County of San Diego, which overlaps the Metropolitan Statistical Area (MSA) of San Diego-Carlsbad-San Marcos.
*Data Source*: Bureau of Economic Analysis, Department of Commerce. Regional Economic Account: Local Area Personal Income. Retrieved from http://www.bea.gov/regional/reis/ on June 18, 2010.

In 2004, the Milken Institute ranked the County of San Diego as the top biotechnology cluster in the U.S. (DeVol et al., 2004). According to this report, San Diego has the strongest R&D capability and also holds high rankings in other areas including risk capital, human capital, biotech workforce, and current impact among all metropolitan statistical areas (MSAs). The analysis done by the Brooking Institution (Cortright & Mayer, 2002), an independent research institute on social issues, also highlights that San Diego is one of the most noteworthy biotechnology centers, which is equipped with both strong research competence and commercial capacity. In terms of employment in the biomedical industry, San Diego is one of the two areas where the ratio of biotechnology employment to manufacturing is more than ten percent. During the past five years – from 2005 to 2009 – biotechnology companies in San Diego absorbed about 14 percent of the total venture capital investments (see Table 4-3). According to a recent survey (Ernst &

Young, 2010), San Diego is the home of 35 public biotechnology companies following only the San Francisco Bay area and New England. According to an industry directory, BioScan, San Diego is home to 131 biotechnology companies (BioWorld, 2010). As shown in Figure 4-8, most of them are located in and around the Scientific and Research Zone in Torrey Pines.

To date, San Diego is drawing much attention from countries and cities around the globe. During the last decades, the area has grown up to be a hub of not only biotechnology industry but also telecommunications and other high-technology sectors. It is a case that illustrates how a community of entrepreneurs, academic scientists and leaders can learn about innovation, cultivate practices of entrepreneurship and nurture a culture of collaborations.

**Figure 4-8.** Locations of Biotechnology Companies in San Diego




*Note:* In the directory, BioScan (2010, August), there exist 131 biotechnology companies in the Country of San Diego, but addresses of two companies could not be traced down.
*Data Source:* BioWorld, 2010.

# CHAPTER 5: LEARNING IN COMMUNITIES

In this chapter, I first discuss the process of biotechnology entrepreneurship. By examining the essence and elements of biotechnology business, I suggest that each start-up is built on pools of skills and expertise. Entrepreneurs and managers must be capable and experienced to carry on their enterprise. In many stages, they need to collaborate with outside experts to supplement internal skills and resources. In this respect, I argue that the source of robust start-up activity is knowledge and practices embodied in entrepreneurs and experts, rather than physical infrastructure or resources. I then present four groups of entrepreneurs, which have spawned many biotechnology companies. Next, I describe the career trajectories of seven interviewees to understand how individuals learn and become entrepreneurs. Drawing on these two sections, I argue that individuals develop knowledge and practices by acting and interacting in communities, by which I mean teams of people working together to achieve goals in common by, usually, forming companies. The fuel of biotechnology entrepreneurship is the learning process in communities of practice. In the following section, I propose three factors – a mass of start-ups where employees developed their skills, an inflow of talent from outside and the local leadership, who promoted interactions across communities – which have been critical to nurturing the biotechnology cluster in San Diego. In the last section, I shed light on the development of business resources – venture capital, angel investments, and specialized services – and a culture of collaboration. Business resources and culture of collaboration were constructed in the process of solving daily problems and sharing understanding through actions and interactions in communities.

## 5-1. Practices of Biotechnology Entrepreneurship

The beginning of the biotechnology industry traces, first, to the coming of new scientific understanding on molecular biology, and, second, to the techniques, institutions and talent, which turned that knowledge into products. In contrast to traditional pharmaceutical companies, biotechnology companies are mostly formed to commercially develop scientific discoveries at universities and research institutions. Therefore, biotechnology companies have to mobilize resources from partners and investors from the beginning to proceed with their development programs. Biotechnology companies should be built on scientific platforms by which they attract talent and finance, and around which they conduct pre-clinical and human clinical tests.

But science is only a part of the entire body of the business. To have their products approved by the FDA and delivered to patients, scientific discoveries go through a ladder of steps, each of which requires a unique set of skills and expertise, and sequences of interactions with multiple partners. The resources necessary to develop a human drug are much beyond what any start-up company and their founders can afford. The business of biotechnology is to attract, organize and engage expertise and resources on the basis of a scientific platform. It is science, but also an art of articulating and communicating their scientific vision, which mobilize resources and skillful professionals for developing treatments. Therefore, forming and running a biotechnology company involve a spectrum of skills – particularly social and narrative skills – and practices in addition to a scientific foundation.

Commonly, scientists who first recognize the commercial potential and possibility of their own research discoveries seek to ways to develop them. Regarding the importance of science in forming and flourishing the biotechnology industry during the 1980s, Byers (1988, p. 116) remarked: "the driving force of this industry isn't finance, and it isn't management. It's science." As the science was exploding and scientists could frequently see their peers venture into the commercial side, Byers pointed out, they "can't help but think: If that guy can do it, I can do it." A large portion of start-ups during the 1980s and 1990s was formed by scientists either from industry or academia as an avenue to pursue commercial development of their scientific ideas. However, a part of start-ups originated from established companies which spun their research program or talent under an independent entity.

The firm at the beginning is a platform to articulate its business plan as well as a legal platform to license and patent technology. For the first year or even following several years, many are still ‘moonlight’ or ‘shell’ firms. These early start-ups exist only on ‘documents and founders' name card, not yet taking any discovery or development activity. One of the first steps these ‘moonlight’ companies take is to establish a legally protectable scientific foundation by licensing and patenting research discoveries. A founder or a founding team usually goes to a technology transfer office at a research university to negotiate a licensing deal. The negotiation for licensing is, as John Stuelpnagel (interview), a founder of Illumina, put it, "an art: it is an art of negotiation; it is an art of contract understanding; and it is an art of subtlety of terms." To license a protectable technology, entrepreneurs need to understand and be able to deal with complex negotiation and legal procedures.

The second step involves writing a business plan and attracting early stage investors. Scientific founders have to compose a line of stories to communicate with potential partners, employees and investors. Their scientific features should be translated into 'benefits' for which consumers are willing to pay, because investors look at marketability rather than scientific perfection in making investment decisions. Writing a good business plan is not about listing scientific features, but articulating them in a meaningful way to investors and partners. It is articulation of "a scientific concept" that is important to investors (Larry Bock, interview). To communicate effectively, writers of business plan should be able to compose their storyline from the perspective of the audience such as potential investors. Founding scientists could learn skills and knowledge to head the development and commercialization activity, or they leave this job to seasoned entrepreneurs or venture capitalists.

The next step involves searching for partners and forming a management team. To most scientists, the commercialization activity is foreign territory, which is why most biotechnology companies are formed by a group of skilled entrepreneurs rather than by a scientific founder. Patricia Lilian (2004), a cofounder of a start-up, Kinexis, in 2002, gave a firsthand account of how her colleagues combined their expertise in founding a company. She was an experienced consultant, so she brought in "management expertise and know-how in drug discovery and development," the other partner provided "the clinical and entrepreneurial perspective" and the scientific founder contributed to its scientific foundation. The importance of an experienced team is indicated in an entrepreneur's remark: "People make or break companies. If you don't have a team that's motivated to get it done, you're not going to get it done, no matter how good the science is." (Jacqueline Johnson, quoted in Fikes, 1994a)

After establishing its legal foundation and forming a managing team, the founders have to get it started by setting up a workshop. A biotechnology entrepreneur depicted the logistics of a start-up:

> To the first year of a biotech company, the greatest roadblock to progress isn't the science. It's usually the logistics of forming the company, getting labs built and outfitted, hiring scientists, getting them in, getting them to work as a team, having them focus on the projects, converting the academic culture from which they probably come to a commercial culture that respects timelines and budgets. (Frederick Frank, 1988, p. 117)

Tony Hunter, who cofounded a biotechnology company (Signal), noted the role of her partner in organizing an array of activities: "Her experience in setting up companies was very important to us, in getting new space, arranging with contractors to do renovations and a variety of things that needed to be done to get us up and running." (Fikes, 1994a) Tina Nova, CEO of Genoptix and a Hybritech alumnus, said of her passion, skills and experience of starting up biotechnology companies:

> There was nothing there. I had to start with everything… hiring people, lab space, lab equipment, employee manuals, everything we needed… The whole idea of going back and doing what I had done before seemed so exciting. I knew I could do it better a second time than I did the first time. (Fikes, 1993c)

There is no standard process or formalized protocol in establishing start-ups and proceeding with these early logistics. To be a competent start-up entrepreneur, as Tina

Nova indicated, individuals having entrepreneurial passion have to be involved in the process. Larry Bock (interview), a venture capitalist, who created a few dozen start-ups, described how entrepreneurs learn to be a path-master:

> When you start up a company, to an entrepreneur, it looks pretty easy. To other people, it is daunting. They even don't know where to get started. If you look at entrepreneurs' prior tract record, they have a history of starting up stuff from scratch... It sounds simple, but people just don't know where to get started. In some cases, it's a series of baby steps, but they know what those steps are to be taken to create something from nothing.

Once founders set up a laboratory and lay down a scientific foundation through patenting or licensing, they need to proceed with their scientific program by bringing in scientists, motivating them to work, composing an advisory board and collaborating with outside organizations. As shown in Table 5-1, the drug discovery process involves a series of distinct procedures. During this discovery process, the primary concern is whether the company could prove its scientific concept and proceed with its research program as planned. To a large degree, the success of raising early-stage capital, called ‘pre-seed’ and ‘seed’ funding, is contingent on whether a start-up has accomplished its early scientific milestones. In the words of an entrepreneur, Jacqueline Johnson, investors "want labs up and running, research programs outlined and functioning and objectives being met" at this stage (Fikes, 1994a).

**Table 5-1.** Drug Discovery Process

| Phase | Description | Involved Techniques & Disciplines |
|---|---|---|
| Pre-discovery | Understand the disease | |
| Target Identification | Choose a molecule to target with a drug (A target is generally a single molecule, such as a gene or protein, which is involved in a particular disease) | |
| Target Validation | Test the target and confirm its role in the disease | Genomics, Proteomics, System biology, RNAi |
| Drug Discovery | Find a promising molecule (a "lead compound) that could become a drug | |
| Early Safety Tests | Perform initial tests on promising compounds (Scientists test Absorption, Distribution, Metabolism, Excretion and Toxicological properties) | |
| Lead Optimization | Alter the structure of lead candidates to improve properties | rDNA, MAb, Rational drug design, Combinatorial chemistry, High throughput screening |
| Preclinical Testing | Lab and animal testing to determine if the drug is safe enough for human testing | |

*Source:* Pharmaceutical Research and Manufacturers of America (PhRMA), 2007, p 2-5; Pisano, 2006, p. 46.

After completing the discovery process, biotechnology companies enter into a series of lengthy and costly human clinical trials, and file a new drug application to the FDA for an approval. Prior to the clinical trials, biotechnology companies should receive an approval to go ahead with human clinical testing by the FDA and a clinical research review board of clinical testing organizations. The clinical trials investigate the safety and efficacy of drug candidates in humans. If the trials indicate the safety and efficacy of a compound, they file the new drug application to the FDA. The clinical testing is conducted at several clinical testing organizations, mostly hospitals, across the country or even around the globe. The success much depends on how a management team designs their clinical trials and maintains communication with multiple groups of experts including the FDA, clinical trials hospitals, researchers and physicians.

Proceeding with clinical trials and dealing with regulatory affairs is the most complex, complicated and costly part of the entire process to biotechnology companies and entrepreneurs. Dennis Carson, director of UCSD Cancer Center, did early stage clinical trials for a cancer drug on his own during the 1970s. He said of the difficulty:

> It is extremely difficult to do what I did, nowadays. I made the drug myself, I designed the trial myself. You can't do this nowadays, because there are so many hoops to go through and the costs are incredible. There is more paperwork in everything now, because of litigation, and more and more regulations. (Broderick, 2007)

Moreover, clinical trials consume a large part of the entire cost. According to a recent analysis by DiMasia and Grabowski (2007), the costs of the human clinical trials account for almost two-third of the total spending (see Table 5-2). In addition to the cost, the process takes, on average, almost seven years.

**Table 5-2.** Capitalized preclinical and clinical period & costs per investigational biopharmaceutical compound

($ millions of 2005 dollars)

| Testing phase | Expected out-of-pocket cost | Phase length (mos.) | Monthly cost | Start of phase to approval (mos.) | End of phase to approval (mos.) | Expected capitalized cost |
|---|---|---|---|---|---|---|
| Preclinical | 59.88 | 52.0 | 1.15 | 149.7 | 97.7 | 185.62 |
| Phase I | 32.28 | 19.5 | 1.66 | 97.7 | 78.2 | 71.78 |
| Phase II | 31.55 | 29.3 | 1.08 | 78.2 | 48.9 | 56.32 |
| Phase III | 45.26 | 32.9 | 1.38 | 48.9 | 16.0 | 60.98 |
| Total | 169.0 | 133.7 | | | | 374.70 |

*Note*: All costs were deflated using the GDP Implicit Price Deflator. Expenditures capitalized forward to the point of marketing approval for a representative time profile at an 11.5% real discount rate. The estimated length of the approval phase is 16.0 months.
*Source*: DiMasi & Grabowski, 2007.

To maneuver the series of clinical trials, entrepreneurs and senior scientists need to communicate seamlessly with the FDA and physicians as well as have understanding and insights on their science and clinical designs. A senior manager, Faheem Hasnain, vice president of the oncology rheumatology strategic business unit at Biogen Idec's San Diego research center, said of the difficulty: "you have to bring ten products to the clinic to see one come to market. To play this game, you have to be disciplined and smart about using biology to design your clinical trial program" (Broderick, 2007). Many entrepreneurs of the biotechnology industry move on to the next phase of clinical testing ignoring warning signs from their earlier clinical trial rather than discontinue their development effort. The mistakes are due to either a fear that any negative news would collapse their venture or their lack of expertise (Webb, 2002a). During the early 1990s, waves of failed clinical tests at their late stage raised public concern to a considerable level. The Economist (1994), a weekly journal, attributed these failures to scientist entrepreneurs' lack of experience and discipline: "In many cases the blame lies with inexperienced managers, often ex-scientists, who have tried to rush products through the tedious regulatory process to meet self-imposed deadlines."

As important as scientific insights and disciplined decisions, communication and engagement with the FDA and outside experts is critical to designing and interpreting clinical trials effectively. Early communication and collaborations with these groups of authority and experts are essential to reducing ambiguity and cost involved in the drug development process. This is why the biotechnology and pharmaceutical industries have been involved in discussions and debates with the Congress and the FDA to widen the communication channel between industry and the regulatory agency. Regarding how the FDA committed to heightening communication with companies in 2003, Carl Feldbaum, president of the Biotechnology Industry Organization (BIO), noted:

> The FDA has pledged to work with the small companies and large companies to make sure in the interim between Phase II and Phase III, that the companies know exactly what is expected of them from the FDA and the FDA writes it down, commemorates it and sticks to it, to use a football analogy, so as the Phase III clinical trial proceeds they don't keep moving the goalposts. (Webb, 2003a)

Yet, effective communication and interactions require sophisticated skills, experience and relationships to be taken place. As David Hale noted, "I think sometimes it's difficult to know what the FDA is really asking for and sometimes it would be good to be able to debate issues to hopefully find a better solution" (Webb, 2004).

Experience and expertise of communicating and collaborating with the FDA and outside experts are also indispensible in filing a new drug application for the FDA approval. Amlyin's case illustrates how this company and its managing team were engaged with the FDA related to their diabetic drug, Symlin – Amlylin was founded and started to develop a diabetic drug in 1987 and the company received the FDA approval for its diabetic drug in 2005 – as written in San Diego Union-Tribune:

> To deal with the FDA, Graham [Amlylin's CEO] pulled together a team of Amylin's top executives and talks during which the company people tried to persuade the regulators to read the results from Symlin's clinical trials the way the company read them. Amylin enlisted the help of some of the nation's top endocrinologists. (Somers, 2007a)

Overall, only skilled and experienced entrepreneurs could handle the process from incorporation to a new drug application.

Besides steering through the process, entrepreneurs have to lead efforts to secure financial resources. To proceed with their discovery and development program, a management team has to constantly interact and inspire investors, corporate partners and the public. In an analysis of therapeutic compounds that first entered human clinical testing between 1990 and 2003, DiMasia and Grabowski (2007) found that it took, on average, about 11 years with a cost of $374.70 million to develop a drug (see Table 5-2). They also found that the probability that a compound already entered into Phase I clinical trials would receive the FDA approval was 30.3 percent. If the success rate of 30.3 percent is taken into account, the total cost per an approved therapeutic compound was estimated $1,241 million. Since it takes more than ten years before a start-up completes its development process and earns revenues, it has to continuously raise capital for, at least, a decade. Prior to gaining the FDA approval, biotechnology entrepreneurs have to sell their vision of science by composing narratives and conversing with potential investors.

The primary sources of capital change as a company moves along the development stages, and the rounds of financing before going to the public market are named as Series A, B, C and so on as it goes further. During the early-stage of exploring and validating its scientific foundation – it is termed proof-of-concept (principle) – a company depends mainly on angel investors, foundations, research grants from the federal government and early-development grants from the Small Business Innovation Research (SBIR) program. During the earlier stage without any data from clinical trials, entrepreneurs can only draw on a storyline of their scientific concept and credibility of their scientific advisory board in attracting investments. As the company proceeds with its program, entrepreneurs heighten reliability and credibility of their narratives by matching their achievements with their plan. With their stories, entrepreneurs should be able to communicate their vision and potential with communities of investors in a way that makes the listener want to participate in the adventure. Since effective communication take place under a condition in that both sides stand on a shared understanding and have a long-term relationship, a capable start-up and its entrepreneurs need to not only compose an exciting story, but also keep their stakeholders informed and interested in their story.

As the program advances by successfully synthesizing compounds and completing preclinical testing, the company raises funding from various sources including venture capital firms, private equity firms, the public market and large pharmaceutical companies to conduct human clinical trials. According to an analysis on financing of 88 biotechnology companies in San Diego, the three main capital sources – corporate strategic partnerships, venture capital and public offerings – accounted for 84 percent of the total capital input. (see Table 5-3) If the company completes the initial public offering, from this point it could draw on the public stock market by issuing shares not only at the initial public offering but also at follow-on offerings. While going public provides an important source of funding, it also comes with its own challenges, especially for young start-ups: any public companies have to address complicated regulations and information demands from the public investors. As a third primary source along with venture and equity capital, and the public stock market, biotechnology companies draw on the resources and expertise of large pharmaceutical companies through corporate strategic partnerships. Pharmaceutical companies invest in or pay for discovery programs of biotechnology companies in return for gaining marketing rights for the future drug.

**Table 5-3.** Sources of financial resources

($ millions)

| Type of Financing | Amount | Percent |
|---|---|---|
| Corporate Strategic Partnerships | 482.0 | 35.1 |
| Venture Capital and Other Institutional Private Placement | 386.1 | 28.1 |
| Public Offerings | 278.7 | 20.3 |
| R&D Partnerships | 140.0 | 10.2 |
| Debt | 68.0 | 5.0 |
| Founder/Angel Financing | 10.5 | 0.8 |
| SRIR Grants | 6.7 | 0.5 |
| Total | 1372.0 | 100.0 |

*Note:* The analysis was based on data of funding sources at 88 biotechnology firms in San Diego from 1971 to 1990, which constituted the entire population of the local industry
*Source*: Mitton, 1991.

As physical proximity, presence and shared experience are crucial in communicating the validity of a scientific platform, venture capitalists tend to invest in entrepreneurs whom they trust and like. In this sense, establishing and maintaining relationships with private and public investors and corporate partners is an important part of entrepreneurs' capability. As an executive of an agricultural biotechnology company, Mycogen, described how his company interacted with these investors:

> Even though we have cash in the bank, we're spending a lot of time and energy trying to educate Wall Street about our business. We're probably going to need to raise more money at some point, and if Wall Street begins to understand the profitability of the pesticide industry, the need for new products, and our positioning in the market, we'll be well served two and three years out. (Andrew Barnes, 1988, p. 158)

Corporate partnerships require also long-term interactions and mutual understanding to be accomplished. Corporate partnerships are particularly an important funding source for late-stage clinical trials, and they are a route whereby biotechnology companies access the resources and expertise of large pharmaceutical companies. In this sense, corporate partnerships between biotechnology and pharmaceutical companies are the ways of complementing and supplementing each other's capabilities. To tap into corporate partnerships, entrepreneurs need to interface with pharmaceutical companies and handle any conflicts skillfully. John Stuelpnagel, founder of Illumina, explained the capability necessary to maneuver corporate partnerships:

> Understanding how relationships might benefit and promote the strategy of the company is important. It is also important going out, reaching out and educating potential partners, understanding what their needs are, and ultimately making marriages work for both. (interview)

**Table 5-4.** Skills and practices for founding and running a biotechnology company

| Activity(Stage) | Collaborators & Partners | Skills & Practices |
|---|---|---|
| Pre-Discovery | Academics<br>Early-Stage Investor | Recognizing Commercial Potential & Possibility of Scientific Discoveries |
| Establishment of a Start-up | Tech Transfer Staff<br>IP Attorney<br>Consultant<br>Real Estate Developer | Incorporation (Forming a legal entity)<br>Forming a Management Team & Scientific Advisory Board<br>Licensing (Negotiation) & Patenting<br>Writing a Business Plan (Composing a Storyline for Scientific Concept)<br>Setting up a Workshop (Laboratory) |
| Raising Early-Stage Capital | The NIH (SBIR)<br>Angel Investors<br>Venture Capitalists<br>PR Practitioners | Grant Writing & Application<br>Pitching & Public Relations<br>Communication & Relationship |
| Discovery & Development | Academic Scientists<br>Specialized Companies | Communication<br>Creating a Culture of Innovation |
| Raising Late-Stage Capital | Venture Capitalists<br>Equity Investors<br>Corporate Partners<br>The Public | Establishing & Maintaining Relationships<br>Negotiation<br>Public Relations |
| Clinical Trials | Clinical Trials Org.<br>Physicians | Communication with the FDA & Physicians<br>Designing Clinical Trials<br>Interpreting Data from Clinical Testing |
| Filing for the FDA Approval | The FDA (Staff & Advisory Committee)<br>Advocacy Groups | Communication with the FDA & Patient Advocacy Groups |

*Note:* The activity (stage) does not take place in a linear way. Many partners including IP attorney, PR (public relations) practitioners and venture capitalists become involved in multiple stages, not only in a single activity.

I discussed about the skills and practices necessary to maneuver each stage or accomplish each objective in the process of establishing and running a biotechnology company. (Table 5-4 highlights the skills and practices for each biotechnology activity.) But, it is not only skills and knowing, but also personality, identity and relationship, which account for entrepreneurial competency. Larry Bock (interview), a venture capitalist who has founded or co-founded many companies, presented three characteristics as the essence of a start-up entrepreneur. In his words, entrepreneurs, first of all, are "very scrappy, meaning they figure out how to get the answer in the quickest, easiest and smartest way." As a second element, entrepreneurs have "a high sense of urgency that means they always do it today instead of waiting until tomorrow." Entrepreneurs are the people who are fascinated with the process, and who are "driven somewhat between the balance of the fear of failure and the overwhelming optimism." The last element, said Bock, is 'bankability' referring to the ability of impressing, inspiring any investors to the level that they want to be a part of a venture. A venture capitalist, Andrew Senyei, pointed out the skills and attitude of a successful biotechnology entrepreneur when he was asked why he had been working with an entrepreneur for a long time: "She [Tina Nova] has a combination of what I think is the key to being a success in the biotech space: a deep technical understanding, the leadership and management skills, and she knows how to motivate people and make things happen in a very complex environment" (Somers, 2005).

Entrepreneurs are willing and able to develop their knowledge, practices and identity to tackle the continually rising issues by engaging in a variety of activities for a substantial time length. Successful biotechnology entrepreneurs update and expand their skill set and expertise by situating themselves in diverse social contexts and social groups. Based on the depth and breadth of their experience, entrepreneurs become capable of understanding and maneuvering the process in a better way. These individuals are highly versatile and resilient, so many of them continue founding and running a number of start-ups and some of them become venture capitalists or consultants at some point.

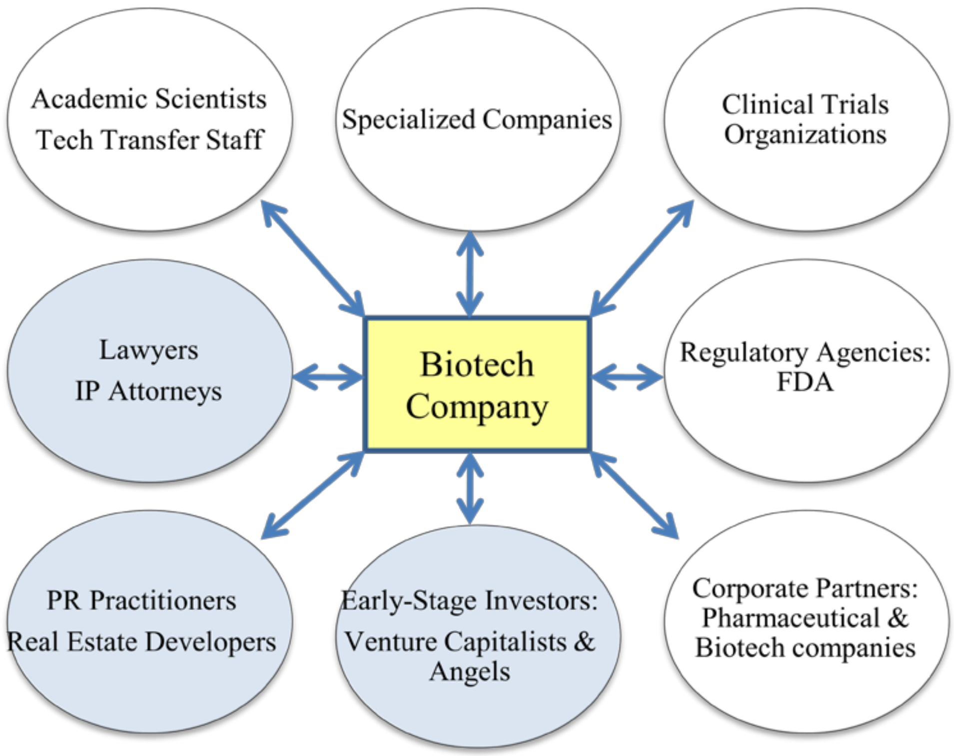
Although many entrepreneurs develop skills, knowledge, practices and identity throughout their life, their specialty and inclination tend to be bounded to a certain activity and a scientific area. Therefore, in forming a start-up and managing a company, several individuals with different specialties and practices join to supplement the necessary skill set. As a biotechnology company moves along the development program, entrepreneurs should adjust and develop their skill set, practices and relationships for different activities. The ability and experience of embarking on a start-up revolve around understanding science, dealing with intellectual property right, incorporating a firm, collaborating with academia and attracting early-stage investors, including angel investors and venture capitalists. As the company moves into the development process, its managing team should be familiar with the regulatory process and comfortable in communicating with the FDA. At this stage, the entrepreneurs are also expected to be able to attract funding through corporate partnerships and the public market as well as venture capital firms. In a case that the company succeeds in receiving the FDA approval and chooses to be in the marketplace on its own, then the managing team should be capable of building faculty and facilities for manufacturing and marketing.

Due to the evolving demands of the biotechnology start-up, and the need for diverse skills and experiences, many biotechnology companies often replace their management team as they move further in the process. As Timothy Harris, CEO of Structural Genomix – a cancer treatments developer – explained why he decided to depart the company, which he had cofounded: "It's a great company and I enjoyed building it to what it is today. But I'm an early-stage guy" (Somers, 2004). He and the board thought "the company needed someone a bit more experienced in commercialization and drug development." Moreover, he wanted to be involved in the early-stage process, as he said: "there's a lot of early stage technology that needs to be prosecuted and I'm quite good at doing it" (Somers, 2004). He resigned to go back to forming start-ups by applying his expertise to discovery-related activity, while the company would recruit an executive having experience in late-stage activities. As this case shows, many companies reshuffle their management team having experience in operations, marketing and sales when they are close or receive the FDA approval (Crabtree, 2005b).

Because the knowledge, practices and resources necessary to conduct the entire process of drug development are daunting for many companies and entrepreneurs, most entrepreneurs specialize in a particular business model or technological platform. To say again, rather than developing skills and practices to work with the entire development process, many entrepreneurs choose to focus on developing their capacity for a specific stage or area for developing drugs. This is why there emerged specialized companies, which focus on specific activities or areas. Between the 1990s and the early 2000s, a number of companies rose to provide research and clinical testing services to drug developers. These 'toolbox' companies focused on developing their faculty for supporting rather than conducting the drug discovery process on their own. Among these companies that were founded to specialize in certain technological or methodological platforms were Ixsys, CombiChem and Applied Molecular Evolution (AME). Contract Research Organizations (CROs) specialize in clinical trials and they provide services related to clinical testing to biotechnology companies. CROs include a spectrum of companies which “toxicology research, preclinical research, clinical research in humans and data management or statistical services” (Ryan Bethencourt, interview). To many biotechnology companies, according to Ryan Bethencourt who is a director at a clinical research organization (CRO) – California Clinical Trials – it is more effective to run clinical trials with the help of CROs than to develop capacities internally. Like 'toolbox' companies and CROs, a breed of specialty pharmaceutical companies emerged in the process of addressing the challenges in developing drugs from the ground. Instead of carrying out the discovery process, specialty pharmaceutical companies choose to license approved drugs or candidates in late clinical trials for marketing, which have been overlooked by large pharmaceutical companies. By the same token, 'virtual biotechnology companies,' which outsource many functions and facilities from outside, emerged due to the difficulties of delivering the entire drug development process. The ‘virtual biotechnology companies’ draw on many specialized companies and service providers in developing drugs, instead of developing and investing in expertise and facilities internally.

To fill their gaps of expertise, practices and resources, most entrepreneurs need to collaborate with multiple groups of experts and supporters. (refer to Figure 5-1.) Each of these groups develops its capacity and practices to support entrepreneurs and biotechnology companies. Among these specialized practitioners and partners, early-stage investors including venture capitalists and angel investors, and specialized service providers like lawyers, intellectual property attorneys and public relations practitioners are especially important to start-up companies and entrepreneurs. Because a large part of funding and supporting flows to start-up companies through in-person interactions and engagements, the number and scale of locally-located investors and specialized service providers are an important element for fostering and stimulating entrepreneurial activity.

**Figure 5-1.** Partners and collaborators for biotechnology business




Among these groups, local investors – especially venture capitalists and angel investors for start-up companies – and specialized practitioners are critical to cultivating biotechnology entrepreneurship by providing seed funding and guidance. Venture capitalists are a catalyst for channeling funding from institutions like pension funds and endowments to individual companies. Venture capitalists should be able to raise capital from institutional funds and, at the same time, to be involved in entrepreneurial activity as supporters, connectors and judges. Most venture capitalists are the people who have an extensive track record, relationship and expertise to deal with both sides: institutional funds and start-up companies. Since investments in companies in the early-stage involve high-risk and high uncertainty, only a limited number of venture capital firms have been active in investing in companies in the early-stage process. Even if venture capitalists want to engage in the early process, many of them are unable to do that because "they don't all have the necessary skills" (Byers, 1988, p. 110). Building on their expertise and practices, "some VCs just do seed deals, some do medium-size series A, some do large series A, some just do follow-on rounds" (Ralph Mayer, quoted in Bigelow, 2009).

Angel and the Small Business Innovation Research (SBIR) funding is the most important financial source for early-stage companies. In the last several years, angel investors, who invest their own funds in start-up companies, have risen to fill the funding and knowledge gaps of early-stage companies. The engagement of angel investors is particularly crucial to newcomers who need in-person guidance and seed capital for proof-of-concept work. In addition, angel investments are also meaningful due to the federal regulations on the Small Business Innovation Research (SBIR) program. To be eligible to the SBIR funding, that is another significant financial source for early-stage companies, companies should be primarily owned by individuals and independently operated with less than 500 employees. The dilemma is that if the early-stage companies succeed in attracting investments from venture capital firms, the venture capital firms take majority equity ownership of the invested companies. In this case, the venture capital-backed start-ups lose their eligibility to the SBIR funding. In the recent years, angel investments have become more important because most venture firms focus more on late-stage companies, which conduct human clinical trials, while leaving many start-ups in the stage of pre-discovery or discovery with little hope of attracting venture investments.

The investors provide not only funding, but also advice and networking opportunities. As an angel investor, Ralph Mayer (interview) who is chairman of the Tech Coast Angels, said, angel investors "know what to look for, they are pretty good at working with people" and "they know more about what business is gonna be like than the entrepreneur does." However, the extent to which biotechnology companies capitalize on the financial resources and expertise of venture capitalists and angel investors is contingent on the quantity and quality of local communities of investors, because trust and long-term relationship from interactions and engagements are an inevitable element in making investment decisions and in providing knowledge. Ralph Mayer suggested the importance of in-person communication: "Face time with the entrepreneur seems to be a necessity in getting investors to write checks. At the Tech Coast Angels, we have found that investors rarely invest unless they have had at least two face-to-face meetings with the company" (Bigelow, 2009). An account by a venture capitalist, Jeffrey Stein who had joined Sofinnova Ventures as a founding partner of San Diego office, also indicates the significance of in-person interactions in making investment decisions:

> San Diego has an incredible abundance of early stage technologies arising from its universities, research institutions and companies, and it is extremely difficult to get an early look at these opportunities without being physically present to meet with the entrepreneurs and hear their stories. (Somers, 2006c)

In this sense, early-stage funding is commonly referred to as 'proximate capital' because venture capitalists "don't necessarily want to get on a plane to travel a lot," (Wendy

Johnson, interview) or "most people like to invest in places which they can drive to" (Ralph Mayer, interview).

Along with early-stage investors, lawyers, intellectual property (IP) attorneys, public relations practitioners and real estate developers are an important component in the development of a biotechnology cluster. These specialized service providers also fill a gap in knowledge and practices of start-up entrepreneurs. They help entrepreneurs deal with issues like incorporating a company, filing patent applications, formulating legal terms for corporate partnerships, rendering storylines of scientific platforms and referring to appropriate partners. A law practitioner, Mike Hird, a partner at a law firm, said of how he had helped a scientist entrepreneur run a start-up: “often you get a scientist off the bench who wants to start a company but hasn't been in the community. I'm able to help that person meet a lot of different folks and figure out what he or she wants to do” (Somers, 2006b).

In particular, patenting-related practices require sophisticated, long-term experience and expertise that are hard to acquire. According to John Wetherell, a partner of a law firm – Pillsbury Winthrop:

> The problem is that IP, especially in the patent area, requires a complex infrastructure...It requires extensive recordkeeping, you have to have highly trained paralegals in place who can deal with foreign filings. You have to have a sophisticated tracking system to keep track of all the dates. (Webb, 2005)

Public relations practitioners help entrepreneurs and scientists communicate with outside stakeholders including investors, the public and corporate partners. Particularly, early-stage companies have to leverage their scientific platform to mobilize resources from outside sources. To achieve this goal, entrepreneurs need to construct narratives and visuals, which help any potential investors, regulatory authorities and the public make sense of their technology platforms and business models. In addition, the time span for developing products is usually more than a decade, so public relations are critical to securing and maintaining supports throughout the entire process. But as Louis Neiheisel, partner of Peter T. Noble Associates, a local design firm, said, scientist entrepreneurs are generally inept in composing their story:

> Often marketing the product is not where their [scientist entrepreneurs] minds are. They're working in the lab where things are pretty definite. From there, marketing or whatever probably sounds like speaking in tongues. Which is fine. That's why scientists do what they do, and not advertising. (Ashmore, 1999)

Collaborations with public relations practitioners help entrepreneurs communicate better, as a venture capitalist, Kerry Dance, notes: "if an entrepreneur has been scrubbed by a professional services group, they're better apt to tell their story" (Beasley-Jones, 2002).

In sum, the business of biotechnology involves an extensive spectrum of skills and practices to proceed with the entire process. It is a process that takes decades and billions of dollars, which has to be mobilized from investors and partners. It is a process that requires continuous, intimate interactions and collaborations between multiple participants: academic institutions, venture capitalists, corporate partners, clinical institutions, regulatory authorities like the FDA, the public and so on. Entrepreneurs need to communicate with these institutions either to attract attention or to negotiate. Troy Wilson (interview), founding CEO of Intellikine, compared the role of entrepreneurs as a conductor of symphony:

> Being successful in a biotechnology company requires you not only to be successful in science and clinical trials, but it requires you to have a business model that matches that and find enough money to be able to accomplish those goals. So, it's really marrying the science with the clinical developments with business and financial piece of it. Bring all those elements together, all working well together like a symphony. That's when really biotech companies are most successful.

In this sense, the core of biotechnology business is a body of knowledge and a set of practices which are developed and embedded in entrepreneurs and specialized practitioners. Among many skills and capacities, most of all, entrepreneurs need to be capable at composing narratives and communicating with multiple partners to bridge the gap of time and resources by impressing and inspiring groups of supporters. It is also the communication and social skills which lessen the ambiguity and uncertainty of the biotechnology business. They also need to be agile in developing other skill sets, understanding and relationships in the process of solving daily problems. Particularly, relationships and narrative skills are critical to communicating with and convincing many stakeholders effectively. The importance of composing a compelling storyline and building relationships is described by Rolf Muller, cofounder of a biotechnology company, Biometrica:

> It is all about the message. You don't get a lot of chances if your message is just wrong even when you talk to the right people. You will not go further. You have to refine your message over all the time. The messaging will never be finished. You always have to work on what you actually want and who you want, and then you get these people… It's all about relationships that gets you message to be crossed in the best way. Because you have no money at the beginning, you have to have a story which makes so much sense that people either want to help you, want to work with you or want to show the right direction. If you don't have the story, you don't get help. (interview)

The biotechnology industry forms and flourishes around the communities of knowledge and practices. From a historical perspective, the industry is the consequence of entrepreneurs' learning process at their clubs, companies and communities, where they interact and practice to solve problems. Thus, knowledge and resources are created and circulated within a locality, where individuals act and interact with co-workers and partners. In this regard, the biotechnology cluster in San Diego is not only a cluster of companies and resources, but a stock of knowledge, a set of practices and shared understanding, which have enabled entrepreneurs and scientists to found start-ups and maneuver the drug development process. This brings us to the subsequent questions: where have the biotechnology companies and specialized service groups come from; how have entrepreneurs and partners developed knowledge and practices?

### 5-2. Formations of Entrepreneurs' Groups and Spin-offs

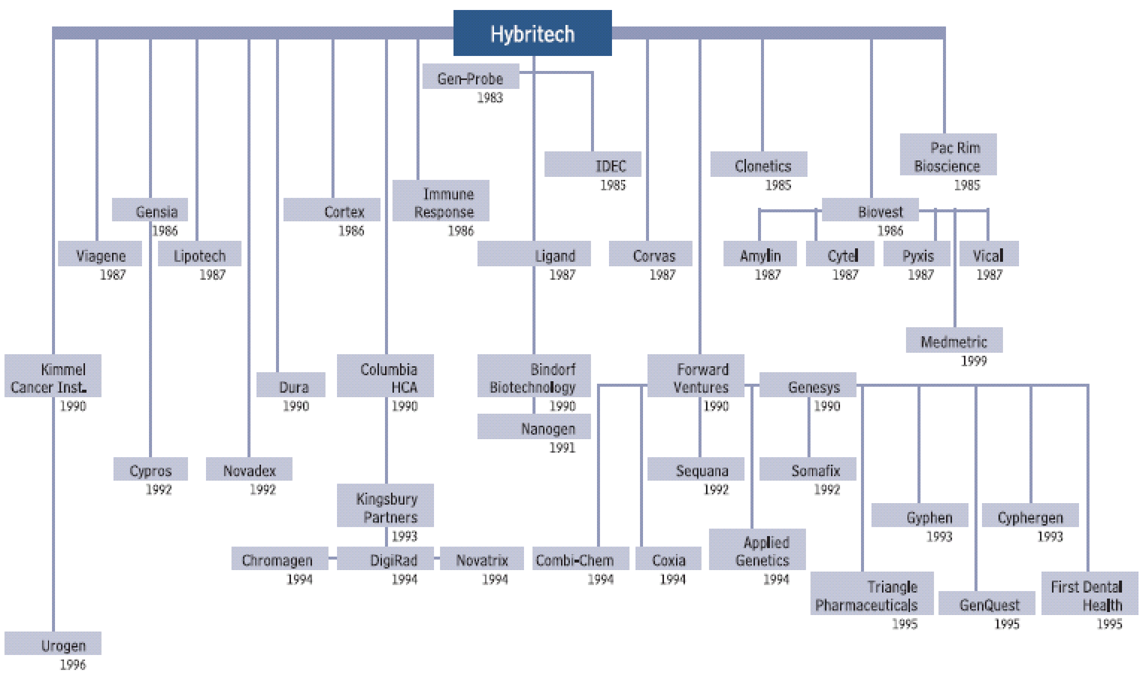
The source of knowledge and practices for founding and running biotechnology businesses is communities, in which participants engage with problems and interact with colleagues to deal with issues on a daily basis. The case of Hybritech's senior managers and scientists illustrates how the learning experience through taking actions and interacting with their colleagues in a community has created knowledge, practices and relationships, which have nurtured many biotechnology companies in San Diego. By capitalizing on their experience and relationships at Hybritech, many senior managers have become skilled and prolific biotechnology entrepreneurs or investors. These people have been involved in founding many biotechnology companies, creating trade associations and initiating collaborative efforts. Among the senior managers of

Hybritech, Cam Garner, director of sales and marketing division, founded several specialty pharmaceutical companies in conjunction with his colleagues and employees in San Diego. In the process of founding and running these specialty pharmaceutical companies, Cam Garner and his colleagues have developed knowledge and practices for the specialty pharmaceutical business. These companies have created thousands of jobs in San Diego, and they present an important part of the biotechnology community in San Diego. Two venture capitalists, Eckard Web and Kevin Kinsella, have been instrumental in embarking on many biotechnology companies. Both of them have developed unique sets of practices for creating biotechnology start-ups respectively, and they have created their learning and practicing communities.

Besides these cases –senior managers at Hybritech, Cam Garner and specialty pharmaceutical companies, Eckard Web and Kevin Kinsella – many communities for learning and practicing have been constituted to address issues together, and many participants in communities have turned into serial entrepreneurs and investors. Individuals who participated in communities at companies and social groups have developed skills and practices by engaging with people and problems. Therefore, the formation and flourishing of biotechnology industry are the result of the learning experience in communities.

Among a number of communities for learning and supporting, senior managers of Hybritech have been the most prolific and influential to spinning off many biotechnology companies. The acquisition by Eli Lilly in 1986 and the subsequent demise of Hybritech became important momentum of spawning many biotechnology companies by freeing a number of seasoned entrepreneurs and their financial funding. In a study of the origins of 68 biotechnology organizations, (co)founders of 13 were tracked to Hybritech by the late 1980s (Mitton, 1990). By 2003, about 50 biotechnology companies had roots in Hybritech alumni (Crabtree, 2003), and by 2008 the number of Hybritech spin-offs increased to 175 according to San Diego Union-Tribune (Steele, 2008). Birndorf said of the multiplication process: "I don't know if the company made entrepreneurs or if the entrepreneurs made it magical, but they realized that they could go off and do it again" (Weeks, 2005).

**Figure 5-2.** Spin-offs of Hybritech




*Source:* CONNECT, University of California, San Diego (quoted in 'Council on Competitiveness & Porter, 2001, p. 68).

In the area of monoclonal antibodies, Hybritech was one of the front runners competing with large pharmaceutical companies like Abbot Laboratories. In the early 1980s, Hybritech was the first and the only biotechnology company in San Diego to establish and expand its development efforts from research and regulatory affairs to sales and marketing by successfully developing a stream of diagnostics. In contrast, during this time period, most start-ups did contract R&D work for large companies or sold out their technologies. Senior managers and some employees of Hybritech had the opportunity to get involved in many important activities of biotechnology business, since the company made "a commitment to developing monoclonal antibodies and of retaining the rights to our development" (David Hale, quoted in Berger, 1984b). Along with its expansion, the company continued recruiting young talent across the country. An account of David Hale who came to Hybritech in 1982 as vice president of marketing indicates what the attraction of the small company was:

> Hybritech, which was about three years old at the time, was making such rapid progress. Already it was using monoclonal antibodies in diagnostic tests. At BBL (a division of Beckton Dickinson & Co. where he was working as a general manager), we were doing the same thing but we were way behind. I decided I was young enough that if the company went under, I could always get another job. (Hardie, 1989b)

In the case of David Kabakoff who joined Hybritech at the beginning of 1983 to head its R&D division for developing diagnostics, it was technology and leadership which attracted their young talent:

> Imagine there is an exciting technology, we had excellent investors, we had capital, we eventually had public markets. This company attracted the best people from the whole industry to lead the various activities. It was a very strong, exceptional group of people. Everyone came from good jobs at other companies, we saw the potential, the opportunity in this small company – that it would really build something

> successful. But it was a very extraordinary group. Part of that was the draw of the technology, part of that the leadership of the company, which was very dynamic and persuasive. (interview)

Responding to why Hybritech could attract this pool of talented and aspiring young people, Howard Greene, CEO of Hybritech, pointed to what was happening at the company: "what we were doing was so exciting and interesting, so that we attracted the people from all over the country" (Fikes & Greene, 2008).

Hybritech, as Cam Garner remarked, soon became a workplace filled with "a bunch of brash kids in their mid-30s who had such energy and apparent confidence that they could make things happen" (Crabtree, 2005e). Howard Greene provided an illustration echoing Cam Garner's point of view: "I was the oldest person in the company at the age of 38. One day, we had an open house for a new facility, and invited the mayor… He said to me, 'you guys are a bunch of children. How can you run a company with a bunch of children?' That was us" (Fikes & Greene, 2008). Many young talented people joined Hybritech, and they experienced the joy of running a dynamic biotechnology company as well as a variety of activities and interactions with their colleagues.

By participating in activities of R&D, regulations and marketing, many people, especially senior managers, of Hybritech developed, acquired and shared knowledge and practices of running biotechnology companies. Howard Greene (Fikes & Greene, 2008), at the 30th reunion of Hybritech, referred to two elements as the fuel of their workplace learning: the first element was the science that "served to keep" all employees together by exciting them; and the second element was the leadership which allowed and encouraged "people do their own thing where people trust each other." They needed to be together and focused to make their company successful. Tina Nova, who joined Hybritech in 1984 after finishing her postdoctoral research, remembered the atmosphere of Hybritech:

> We didn't realize who we were rubbing elbows with. We were all in the same boat, trying to make something survive. That's why Hybritech was nice. It was on the road to being a successful company, but hadn't gotten there yet. (Fikes, 1993c)

David Kabakoff (interview) recalled how he had developed insights and learned to be an entrepreneur at Hybritech:

> That [at the beginning of 1983] was a very exciting time because we were one of the first biotechnology companies here. We were pioneers in the field of monoclonal antibodies. That's really where I learned some of the new biotechnology that was able to contribute to the development of very important products. Based on that experience, I was eventually able to move from the diagnostic world into the drug development and biotechnology world, where I've been spending main part of my career.

A scientist, Jacqueline Johnson, who joined Hybritech as a consultant and later became a full-time employee, said of her experience at the company: "It was a great training ground for young scientists. It grew so fast that people were given tremendous responsibility, which in a larger, more staid company we would have never been given" (Fikes, 1994a).

By replicating and repeating what they had done at Hybritech, many employees, particularly senior-level executives and scientists, began to be involved in creating and running start-ups after leaving the company. Hybritech was an exciting and dynamic workplace that attracted young, aspiring talent across the country. The employees participated in a chain of procedures and practices to advance and commercialize scientific discoveries. They interacted with and learned from each other in the process. In 1984, Howard Birndorf departed Hybritech to run a start-up, Gen-Probe. Later on, he continued to found a series of biotechnology companies in San Diego – he was involved in embarking on start-ups like IDEC Pharmaceuticals (1985), Gensia (1986), Ligand Pharmaceuticals (1988), Neurocrine Biosciences (1992) and Nanogen (1993) already by the early 1990s. Brook Byer, a partner at Kleiner Perkins Caufield & Byers (KPCB), pointed to Birndorf's robust interactions with scientists and his experience of establishing many companies as the source of his entrepreneurship: "he's spent lots of hours counseling scientists and others on how to put a company together, helping them through their insecurities. He takes the insider view because he's been there" (Hardie, 1989c). Birndorf was "a sort of venture capital person who was looking at new opportunities," and able to form start-ups to realize scientific opportunities, as observed by Michael Heller (interview) who founded Nanogen with Birndorf.

However, it was after the acquisition by Eli Lilly in 1986 when "bubbles of biotech" began to burst (Walcott, 2002, p. 105). The executives of Hybritech found themselves unfit with the culture of the traditional pharmaceutical company. In David Kabakoff's (interview) account:

> Once the company was acquired by Eli Lilly, we were a hundred fifty million dollar division of four or five billion dollar company, and this group of people just didn't want to sit still as some guys in Indianapolis told us what to do. We had been running basically our own business. Eventually people moved out and the experiences we had gained allowed people to do [their own entrepreneurial activity].

At the same time, they found themselves filled with confidence, entrepreneurial spirit and skills as well as having sufficient financial resources to invest in start-ups. At that time, San Diego lacked management talent who could steer fledgling companies to the further stages of development process. Scientists at the local research institutions were eager to partner with the former Hybritech executives to commercialize their laboratory discoveries. One by one, the senior managers and scientists left to join or form biotechnology start-ups mostly in San Diego.

Howard Greene and Timothy Wollaeger, a chief financial officer of Hybritech, resigned to launch a venture capital firm, Biovest Partners on October, 1986. In a remark of leaving the Hybritech division, Howard Greene told: "I'm happiest working with a small group of people focused on a challenging technical and marketing opportunity. I'm not a big company man" (Kraul, 1986). The venture capital firm soon raised a $6 million funding primarily from the early Hybritech investors. They provided the seed-funding for six biotechnology start-ups – Cytel, Vical, Pyxis Corp, Amylin, Biosite Diagnostics in San Diego and Neurex in Palo Alto – that were formed by 1988 (Wells, 1988). But soon they wanted to run start-ups as CEOs rather than being venture capitalists. They decided to go back to be entrepreneurs by disbanding Biovest Partners in 1989. Regarding this decision, Timothy Wollaeger said: "I'm not quite sure we consider ourselves venture capitalists as much as entrepreneurs with some start-up money. Building companies is an art. That's what Ted (Howard Greene) and I feel we can do" (Perry, 1989a). Howard Greene described that he was "much more inclined to be working in the lab with the scientists to get something going" (Perry, 1989b) because what he liked to do was running start-ups. Howard Greene joined and led Amylin – it would receive the FDA approval for its diabetic treatment, Symlin, in 2005 – as its CEO until 1996. Timothy

Wollaeger became involved in managing a company, but in 1994, he founded another venture capital firm, Kingsbury Capital Partners. In 2002, he joined a Silicon Valley-based venture capital firm, Sanderling Ventures, as a founding manager of its San Diego office.

David Hale described a similar experience at Hybritech under the control by Eli Lilly:

> After you've been involved in an independent venture like Hybritech, it's hard to go back to being part of a large corporation. Most of the decisions were made at Lilly's headquarters in Indianapolis. Decisions we used to make at Hybritech in a number of weeks took Lilly a number of months. (Hardie, 1989b)

David Hale left the merged company in 1987 to lead a fledgling company, Gensia Pharmaceuticals, attracted by his "strong desire, the dream to get involved in a start-up" that he could build and execute (Rose, 1987). He went on to serve as CEO for four companies including Gensia Pharmaceuticals after leaving Hybritech. Dennis Carlo, a director in charge of therapeutic R&D at Hybritech, participated in forming Immune Response with a group of scientists including Jonas Salk, the founder of the Salk Institute, to develop an AIDS vaccine in 1987. David Kabakoff, director of R&D division developing diagnostics, resigned from Hybritech 1989 and led several companies. Tina Nova who came to Hybritech as a junior scientist in 1984 finishing her post-doctoral work left to join a start-up in 1988. She decided to leave Hybritech because of the departure of her senior associates: "what was hard for me was that the people I admired most started leaving… A year later, I looked up and saw none of the people I respected most. They were leaving and doing new ventures, so I got the bug" (Fikes, 1993c). She moved along three companies before becoming the founding CEO of a cancer diagnostics developer, Genoptix Medical Laboratory in 2000.

It is not only the senior managers at Hybritech who have spawned start-ups, but many employees have contributed to multiplying biotechnology ventures with their own specialty. Hybritech was the magnet for young talent and the nursery where their employees learned skills and developed practices. As the company continued to grow, their workers participated in and observed a variety of activities. As a group at an ascending but still vulnerable venture, many employees felt a sense of community as well as urgency, which facilitated interactions and communication with each other in overcoming many obstacles. In this process, many of them developed mutual trust and relationships. Although they did not recognize it at that point, many of them developed their identity as start-up entrepreneurs. But they had to experience ups and downs by moving across at least a few more companies before turning into masterful practitioners of the biotechnology business. However, senior managers have constituted the core group, which have been critical to expanding the local biotechnology cluster. Overall, Hybritech created a dynamic space, where a group of executives developed knowledge and practices through taking actions and interacting with each other to solve daily problem and address many issues. In the process of doing and interacting, they developed relationships and identity as independent entrepreneurs.

Among the many Hybritech alumni, Cam Garner illuminates how a group of entrepreneurs deepens and broadens skills and acumen by engaging with problems and people. His history also shows how a group of entrepreneurs multiply start-ups through applying learned expertise and practices to founding a series of start-ups based on a certain business platform. Cam Garner, director of sales and marketing division at

Hybritech, remained with Eli Lilly for a year after the 1986 acquisition. Disliking the bureaucracy of a large pharmaceutical company, he left to work at small companies. In 1989, Cam Garner landed at Immunetech Pharmaceuticals, lured by David Hale. Instead of participating in managing Immunetech Pharmaceuticals, Cam Garner took a role of running its small subsidiary, Dura Pharmaceuticals, whose focus was marketing allergy and asthma drugs. In the following year, Immunetech Pharmaceuticals failed to receive its highly anticipated FDA approval. In the process of restructuring, the company changed its name as Dura Pharmaceuticals transforming itself to be distributing and marketing oriented (Douglass, 1990; Rose, 1996b). In 1990, Cam Garner became CEO and led efforts to turn the company into a ‘specialty pharmaceutical company’. Instead of developing therapeutics, the company shifted its focus to identifying already approved but underutilized drugs for allergy, asthma and respiratory diseases, and licensing them in from outside developers.

Dura Pharmaceuticals became a profitable 'specialty pharmaceutical company' in the following years by successfully licensing in a set of drugs. In the process, Cam Garner and his management team developed their expertise and insights into a new business platform – the specialty pharmaceutical model. The core of this business model is to discover and purchase approved drugs or drug candidates in the late clinical stages to serve neglected market sectors by large pharmaceutical companies. Specialty pharmaceutical companies have their core capacities in marketing and distributions for their target area without any significant function in research and development. In 1997, its chief financial officer (CFO), James Newman founded a spin-off, DJ Pharma, by emulating Dura Pharmaceuticals' model (Webb, 1998; Gibson, 2000). In 2000, Dura Pharmaceuticals was acquired by a large pharmaceutical company, Elan, at $1.8 billion. In the same year, DJ Pharma was also acquired by another pharmaceutical company for around $200 million.

Soon after Dura Pharmaceuticals' acquisition, Cam Garner and his management team at Dura Pharmaceuticals embarked on establishing a series of specialty pharmaceutical companies. In 2001, Cam Garner formed a start-up, Xcel Pharmaceuticals, with senior managers of Dura Pharmaceuticals by focusing on neurological diseases. In the following year, Cam Garner assumed the role of CEO at another start-up, Verus Pharmaceuticals, having its concentration in pediatric allergy and asthma. In 2004, Cam Garner founded Cadence Pharmaceuticals specializing in promoting, marketing and distributing products to hospitals. During 2007 and 2008, he cofounded three more specialty pharmaceutical companies with his colleagues at Dura Pharmaceuticals or its spin-offs. (see Table 5-5)

**Table 5-5.** Specialty pharmaceutical companies founded by Cam Garner and his colleagues

| Companies | Year founded | Founding CEO | Specialization | Situation |
|---|---|---|---|---|
| Dura Pharmaceuticals | 1989* | | Allergy, asthma, respiratory | Acquired for $1.8 billion in 2000 |
| DJ Pharma | 1997 | Jim Newman (CFO of Dura) | Cold, cough, allergy | Acquired in 2005 |
| Xcel Pharmaceuticals | 2001 | Michael Borer (CFO of Dura) | Neurology | Acquired for $280 million in 2005 |
| Verus Pharmaceuticals | 2002 | Cam Garner | Pediatric allergy, asthma | |
| Cadence Pharmaceuticals | 2004 | Ted Schroeder (Director of Marketing Hospital Products at Dura ) | Hospital Products | |
| Evoke Pharma | 2007 | David Gonyer (VP of Xcel) | Gastrointestinal | |
| Elevation Pharmaceuticals | 2008 | William Gerhart | Respiratory | |
| Meritage Pharma | 2008 | Elaine Phillips (VP of technology operations at Verus) | Gastrointestinal, atopic | |

*Note*: Dura Pharmaceuticals was acquired by Immunetech Pharmaceuticals in 1989. Data were compiled from website of each company, articles on news media and directories.

In forming these companies, Cam Garner and his team have drawn on a business platform developed from their experience at Dura Pharmaceuticals. In creating a start-up, Cam Garner starts by forming a management team, then explores which markets and products to focus, and brings in a group of early-stage investors, including himself. Ted Schroeder, CEO of Cadence Pharmaceuticals, said of how Cam Garner persuaded him to be the founding CEO of the company: "Cam just had a concept, and said he'd help me raise the money if I'd be interested in running it." About Cam Garner's relationships with and influence to his fellows, Ted Schroder put in this way: "he's a wonderful mentor. I've never encountered anyone who has worked for him who wouldn't work for him again, and that in any business is pretty rare" (Crabtree, 2005e). In 2005, Cam Garner described how he has built companies and interacted with his cohorts at the companies:

> The most rewarding part of my job is creating a company from the beginning, and through that process, creating opportunities for people to take greater leadership roles. What I would brag about is that since I came to San Diego with Hybritech in 1983, more than 10 people who have worked for me are now running their own companies. (Crabtree, 2005c)

The market opportunities on which the specialty companies were founded have been identified in the process of practicing – doing business activity, addressing issues and problems and interacting to solve problems. Ted Schroeder described how the founding team had chosen the arena of Cadence Pharmaceuticals: "we realized there was a large appetite among venture investors to back a hospital-focused pharmaceutical company" (Wiedemann, 2007). Funded by a group of venture and angel investors, these companies have licensed in drugs, each in their specialized area, and increased the values of companies through developing their sales and marketing faculty. The business model and abilities have been developed in the course of practicing at their workplace and then shared with co-workers.

The spin-offs and alumni of Hybritech have comprised a large part of the San Diego biotechnology cluster, but not every biotechnology company in San Diego has roots in Hybritech. A number of other entrepreneurs have come to or emerged in San Diego from many communities. They have formed their own sanctuary of learning and practicing. Among many groups of entrepreneurs, Eckard Weber and his peer group provide an illuminating episode for another pattern of localization. Weber (interview) began his career as a professor of pharmacology at the University of California, Irvine. In academia, he mainly was involved in basic research on drug development and discovery, but he was more interested in "advancing products through clinical development." He was interested in "finding new compounds and drugs that can be used, as opposed to finding new pathways or some genes that might be much farther away from being applicable to treating diseases" (interview).

In 1995, Weber left the university and founded a start-up to develop drugs for stroke and pain. It was not successful, but soon he started a second company to develop cancer drugs, which was not successful either. But he referred to the experience as a learning opportunity: "Both of these companies you could say were not very successful but that gives an individual the opportunity to learn a great deal" (Chambers, 2008). He continued to build a number of start-ups, and joined a venture capital firm, Domain Associates, as a partner in its San Diego office in 2001.

He, as a partner of Domain Associates and a serial entrepreneur, has applied a practice in founding start-up companies: identification of an unmet medical need, and then discovery of drug candidates which could address the unmet need and also are already in human clinical trials or close to this stage. He sets up a start-up to license in newly discovered compounds from existing companies as he told in an interview:

> We try to find new drugs that can treat a disease in a novel way, and on which we already have a significant body of information to tell us that the drug is likely be safe and effective based on at least animal models.

At the same time, Weber brought in a seasoned entrepreneur who would take charge of a new venture. His venture capital firm, Domain Associates, leads rounds of investments to finance the multiple phases of clinical development. Along the way, the entrepreneurs at the company seek to discover more drug candidates to license in. They also develop expertise on and scientific insights into its targeted therapies in the process of clinical development.

In 2001, Weber founded a company, Novalar, in pursuit of developing a better dental anesthesia. He got the idea from his dentist who complained about a dental anesthetic injection and suggested he develop a treatment (Somers, 2008a). The dentist clarified the cause and mechanism of the symptom. Based on his survey on drugs, he found a promising drug candidate which had been already in use for about 50 years. He and his dentist patented the compound for treating dental anesthesia and found Novalar. The company remained 'virtual' until Weber brought in a seasoned entrepreneur in 2004 to lead clinical trials. The compound was approved by the FDA in 2008 (Somers, 2009a).

In 2003, Weber licensed in a compound from a Japanese pharmaceutical company, Kyowa Hakko, to develop as a drug for kidney failures. The compound had been initially developed to treat kidney failures of cancer patients from a chemotherapy drug, but the initial developer discontinued the development program. At the time, Weber was looking for a new drug treating kidney problems of heart failure patients. Executives of the Japanese pharmaceutical company mentioned their abandoned compound to him. Discovering the potential of the abandoned drug candidate, he licensed in the compound and founded a start-up, NovaCardia, to develop it. As a co-founder NovaCardia, Randall Woods, put, "Eckard had this uncanny ability to recognize that a drug like KW-3902 that dealt with renal toxicities might have applications in quite different disease indications" (Crabtree, 2006a).

Weber attributed the discovery to his long-term relationships with pharmaceutical companies in Japan. He explained how he could have built the relationships:

> I have visited Japan for at least 15 years on a regular basis, and have established many relationships with Japanese pharmaceutical companies. That is also very important to have personal relationships with those companies and to gain their trust. So, based on these many years of interactions, I have been able to enter the business transactions with Japanese pharmaceutical companies. (interview)

Weber raised funding from a group of venture capital firms including Domain Associates, with which he is affiliated. After completing the phase II clinical trial in 2007, NovaCardia was sold to Merck, a large pharmaceutical company, at a price of $350 million (Somers, 2007b).

The drug development experience and expertise in the field of cardiovascular diseases led the NovaCardia team to launch a spin-off after the acquisition. During the years, the team at NovaCardia developed another compound targeted at cardiovascular disease in addition to the drug for kidney failures, and. Since Merck was mainly interested in the latter compound, NovaCardia's management team licensed the former compound from the acquirer, Merck, and they founded a spin-off, Sequel Pharmaceuticals, on the compound. Through the experience of developing drugs targeted at cardiovascular diseases, the team gained expertise and skills related to cardiovascular treatments. The new product was to treat a different symptom, but in the category of cardiovascular (Timmerman, 2009). The venture capitalists who had invested in NovaCardia were ready to invest in the spin-off: in Weber’s (interview) words, they were "happy to invest again" as the founding team had a good business plan with a new product.

While Eckard Weber and the venture capital firm, Domain Associates, have focused on the late-stage process, Kevin Kinsella and Avalon Ventures have been involved in building start-ups from basic scientific discoveries. In recent years, these two venture firms are the most significant players in the field of biotechnology industry in San Diego. Kinsella moved to San Diego in 1978 and created two computer companies before embarking on the venture capital firm, Avalon Ventures, in 1983. As a partner of the venture firm, he has led efforts to launch over 50 biotechnology and high-technology companies either in San Diego or in other regions (Crabtree, 2005d). Furthermore, his impact is beyond the companies which he created in association with academic scientists and his team. Larry Bock, who worked with Kinsella from 1985 to 1998, has (co)founded about 40 start-ups. (Among these companies, he was the primary founder of about 20 companies either as a member of Avalon Ventures or of other venture firms.) John Stuelpnagel, who had worked with Larry Bock at Avalon Ventures for a few years, cofounded Illumina – one of the leaders in genomics – and is in the process of forming another start-up by employing 'the Avalon business model'.

The core strength of the group is Kinsella’s and his group's practice of the ‘cocktail napkin start-ups' whose founding ideas came from instructions "over cocktail napkins by some of the world's great thinkers" (Fisher, 1996). As Kinsella said, "we'd much rather get involved earlier so we are part of the creative process, so we can figure out what is the opportunity and who needs to be involved" (Crabtree, 2005d). Kinsella explained this practice:

> One of our distinguishable competencies is, I found, that we read the primary literature in the field. We read scientific journals like Science, Cell, P.N.A.S. [Proceedings of the National Academy of Sciences]... If we find something interesting, we call up the authors. In many cases, in the articles there is called discussion before the end. It mentions the commercial aspect of the technology and that's exactly what I'm interested in. I will call up and at the end of the conversation, I will find out if they agree with what I think it applies and it does. I will try to explain and see him. A relationship is developed, and getting these people involved in the company. They know other people in the field, and they suggest them. (interview)

Larry Bock described this practice: "We'd go everywhere and talk to leaders in the field, and then ask them who they thought the ten leaders in the field were, and then we'd talk to those leaders. From there, Kevin would germinate the basis of a company" (Crabtree, 2005d). In the course, they became skilled at "aggregating intellectual property from multiple academic institutions to create a critical IP (intellectual property) mass as a foundation for a company," as John Stuelpnagel (interview) explained. After running into technological opportunities, the group builds management teams and forms financial coalitions with other venture capital firms.

Regarding the reason for the venture group's success, Kinsella (interview) pointed out their approach to and expertise of selecting projects. In making a commitment, the team asks these questions: "Is this clever enough? Is the timeline short enough? And is the amount of money controllable?" His group has developed ability to recognize talented people and perceive the value of technology in the early-stage. As he said, "it is really important that you know the technology and good people." He ascribed the development of knowledge and insights to experience: That's what experience is: doing things over and over. If you are in a field, and you're doing well, you're gonna acquire expertise over time." To the question of how partners at Avalon Ventures interact with their colleagues, Kinsella answered by giving this account:

> It's all personal interaction…. Jay Lichter [a partner at Avalon Ventures] and I probably talk everyday in the morning. We were probably exchanging 20 or 30 emails. When we were both in stage, the chances are maybe we needle together. Then, you get to know how they think about. It's just a way that one works with anyone that you are close and spend a lot of time with. (interview)

These four groups of entrepreneurs – senior managers at Hybritech, Cam Garner, Eckard Weber and Kevin Kinsella – shed light on the impact and influence of skillful practitioners on cultivating the learning process of their peer groups as well as spawning and nurturing entrepreneurial activity. (Table 5-6 summarizes the specialties and business practices of these four communities of entrepreneurs.) Furthermore, the cases suggest that it is communities – groups of entrepreneurs, investors and scientists who interact with each other to deal with ongoing problems either as a team at a company or a team across companies – where participants learn the craft for building, running biotechnology businesses through doing and interacting. Companies create the space in which group of individuals – mostly senior managers and scientists – constitute communities for learning and supporting in the process of addressing daily issues together. A company is where its executives and employees live and work every day encircled by issues and problems, and they have to improvise and implement solutions to be successful (or sometimes to survive). In addition, companies provide a ground wherein many stakeholders including executives, investors, employees and outside partners are inter-related through shared goals, meaning, experience and practices, which enable them to have seamless interactions and communication. Not only do they put ideas into practices, but they also engage with each other in their everyday life. In the process, as David Kabakoff (interview) put it, "people learn out of their jobs and get the training." It is the multiplying process as "success breeds success," in the words of Kabakoff. He attributed the proliferation process to the learning and becoming experience at companies:

> I think once people have seen or participated in a success, then they have the confidence to try again. And there have been a number of very successful companies here. There've also been companies that have failed to achieve their goal.

Successful companies are crucial in generating financial resources and boosting confidence as well as enabling its employees to experience the complexities of the social reality. Asked why there are so many biotechnology companies in San Diego, Larry Bock (interview) responded by citing the case of Hybritech:

> Have you ever seen the Pythagoras tree [family tree] with Hybritech? It only takes one success in an area in order to get a cluster. So, you could have all the other elements of cluster like a university environment, financing and so on, but until you have one success story, you would not have a cluster. That company then has to spawn all the rest.

But failed companies also provide learning opportunities to their employees. The fuel of entrepreneurial activity is, most of all, the learning experience through participating in communities, which are formed around companies – either at or across companies - and also based on other social and cultural enterprises.

**Table 5-6.** Four groups of entrepreneurs and their business practices

| Leader(s) | Practices (Specialty) | Spin-offs |
| --- | --- | --- |
| Managers at Hybritech | Founding & Running Start-ups Drug Development Activity | About 175 (by 2008) Companies |
| Cam Garner | Specialty Pharmaceuticals: Formation of A Management Team→ Identification of Underserved Drugs→ Opening (Expanding) a Market (Customers) | At least 8 Companies: Dura Pharmaceuticals, Xcel Pharmaceuticals, Cadence Pharmaceuticals |
| Eckard Weber (Domain Associates) | Domain Business Model: Identification of Unmet Medical Needs→ Finding Drug Candidates→ Clinical Development | Dozens of Start-ups: Novalar, NovaCardia, Novacea, Sequel Pharmaceuticals |
| Kevin Kinsella (Avalon Ventures) | Avalon Business Model (Cocktail Napkin Start-ups): Identification of Basic Discoveries by Reading Academic Journals→ Communication with Academics→ Recruitment of Experienced Managers & Scientists to Build Start-ups | More than 50 Companies: Athena Neurosciences, Sequana Therapeutics, Vertex Pharmaceuticals, Illumina |

**5-3. Learning to Be Entrepreneurs**

Employees at small biotechnology companies, having participated in a variety of activity ranging from laboratory science to regulatory affairs, can develop knowledge and practices necessary to tackle obstacles and drawbacks. In developing knowledge and putting it into practice, many of them have become competent and familiar with what they were doing. The practices involve the logistics of forming a start-up, securing intellectual property, conducting clinical trials and raising capital. Most of all, the core part of their competence was derived from what their company and companions specialized and practiced. By participating in managing the biotechnology business process, executives and employees gain insights and perspective on technology and market. Moreover, they develop relationships with the communities of investors, academics and specialized practitioners. It is this learning experience of individuals through participating in communities, mostly, at small companies, that primarily has fueled the proliferation of biotechnology companies in San Diego.

However, we need to look into how individuals learn by engaging with people and problems, and how they experience their transformation into an experienced entrepreneur in communities. To explore how individuals proceed to be capable and devoted entrepreneurs, I first describe a fledgling entrepreneur who entered into the business world just a few years ago. Raj Krishnan and fellow graduate students at UCSD founded a start-up, Biological Dynamics, in hopes of developing early cancer diagnostics around 2007. He wanted to be an entrepreneur who does "something that helps the world" by translating laboratory technology into products (Raj Krishnan, interview). Based on his experiments of isolating DNA from blood samples, he decided to start a company which would apply this discovery to cancer diagnostics. As a first step, he visited the Technology Transfer Office at UCSD to license this technology. After setting up a 'shell' company, he and his colleagues focused on garnering more data supporting their idea – for proof-of-concept. But to Krishnan, "starting a company was as hard as curing cancer" as he put it. This is because entrepreneurs "have to raise a significant of money to build your device, so that they can prove it to people, but at the same time, they have to raise money to do a lot of proofs in trials." As the founding team consisted of graduate students in engineering, they decided to hone their skills for the writing and pitching business plan in order to attract funding from early-stage investors.

His team applied for the UC San Diego Entrepreneurial Challenge to compete with their business plan, but they failed. Ray Krishnan recalled the experience of failure: "we completely got destroyed. Nobody liked our stuff. We got horrible scores. The judges seemed to say 'what is this?" In the following year, they went to the von Liebig Center which provides advisory services and seed funding to UCSD members, and there they met two of the center's advisers, Steven Flaim and Hal DeLong. Krishnan described how his team started to learn how to compose and present a business plan with the help of the center's advisers:

> There, we met Steve Flaim and Hal DeLong. They helped us refine the final pitch a little bit. Once we knew what it is they want to see, we understood and learned quickly as scientists and Ph.D. students. Once we understood what it is they wanted to see and what we had to do, then it was very easy for us to put it together in the slides and present. We went back and tried again. This time, we started winning. (interview)

Stephen Flaim recalled his first meeting with Krishnan at the center, where Krishnan began to explain the discovery and his plan to commercialize it: "it was a really interesting idea and he had data," but he was more impressed by Krishnan's personality (interview). To Flaim, Krishnan was excited and passionate throughout the meeting. Flaim brought in Hal DeLong, an expert at the diagnostics:

> Hal and I advised him how to put together his slide pitch basically. Raj was very good. He listened to what we said, he made changes. He was very coachable. And then, he got to the point. He had a really good slide pitch. Then, he started talking to a few people. Of course, to everybody, this was fantastic. He started attracting attention. (Stephen Flaim, interview)

They continued to help Krishnan and his team by arranging meetings with companies having interest in Biological Dynamics' technology. During the last few years, the team of Biological Dynamics won several of awards and raised sufficient money “to do a lot of proofs in trials” (Flaim, interview) from corporate partners and angel investors.

Krishnan’s faculty adviser, Michael Heller, observed the learning trajectory of his students, the Krishnan’s team, as like the follows:

> Actually one of the things that they did right was this going and talking to so many people, getting help from the experienced: talking to venture capital people and a lot of other people that have started a company, and that were at CONNECT. In a year, they got a huge education of how to do this thing: learning along the way and honing the skills and their business plan. It was a learning process that might take a decade. They compressed them all down in personal initiative to do it. I was amazed because I could see their level of sophistication go up and up. That was a year or a year and half process to do that. (interview)

Their learning has taken place whenever they participated in activities like business competitions and engaged in talks with the experienced. The seasoned people "know exactly step-by-step the process supposed to go through" and "everybody knows everybody," Krishnan said (interview). Therefore, in the words of Krishnan, "if you get somebody who is well connected, he can put you in touch with a lot of people. If you impress people, they would take your name and pass it to their friends who pass it to their friends before you know." In this way, Krishnan and his team have built their network for advice, learning and funding as well as their enterprise.

Philip Low, who won first prize at the UCSD Entrepreneur Challenge in 2008 (the year Krishnan’s team “got completely destroyed) has a similar story. His success at the business competition was preceded by a few years of familiarizing himself with the culture and context of biotechnology start-ups. In 2007, he formed a start-up, NeuroVigil, in La Jolla. At the Salk Institute, Philip Low as a doctoral student did research on an algorithm analyzing sleep patterns. Still a graduate student, he was encouraged by colleagues and advisers to start a company which would develop medical devices monitoring and diagnosing sleep patterns at home (Darce, 2010). Based on his research, he wrote a business plan in 2006, but he soon realized that "it was not enough to have good science" because how the market works is quite different from how scientists approach to research projects. So, he "decided to educate" himself in his words:

> I spent a lot of time in Silicon Valley. I took 19 trips in 2008. I wanted to find the best possible investors, the best possible clients, the best possible teams, the best possible scientific partners, not only in the Silicon Valley, but all around the world. Half of my time was in Silicon Valley, the rest one was elsewhere. (interview)

Through interactions and observations, he learned how the Silicon Valley community operates and how it is different from the San Diego community. But more importantly, the experience gave him training which, he said, enabled him to look at his technology "through investors' eyes as opposed to just scientists." As another effort to educate himself, he reached out to people who could advise him and "who have done this before." These were the people who had built science-based commercial ventures before, so they were able to understand what promises and problems his venture had. One of these people was Irwin Jacobs, founder of Linkabit and Qualcomm. He told how his meeting with Irwin Jacobs encouraged him: “I was very surprised when Irwin told me: 'you have done everything right. This is the way to do it. Grow organically.'” (interview) In an interview, Irwin Jacobs explained how he interact with and guide young entrepreneurs:

> I often talk to someone who comes up afterward [lectures or seminars]. I usually open to conversations... I think the best kind of guidance is really examples. I talk about how I had run both Linkabit and Qualcomm, type of leadership, how they

> [should] run and grow their business. Mostly it is doing things [that] you think is right, as opposed to try to read books and follow some business plan A, B and C, which change every few years. (interview)

In contrast to Krishnan, Low did not draw on programs of CONNECT or UCSD, but capitalized on interactions with veteran scientists and entrepreneurs to educate himself on his own. He could connect with seasoned entrepreneurs because San Diego was small, open community where everybody knows everybody. He decided to locate his business in San Diego because he "knew the people" and San Diego had "some of best neuroscientists" and wireless technology. Recently, he was honored as one of top young innovators by the magazine, MIT Technology Review. He (interview) described his experience of becoming an entrepreneur this way: “Part of being an entrepreneur is about imposing your will on the world. It is recognizing what the world needs and you have the solutions for it.”

As a first-time entrepreneur, Low has acquired perspective and guidance by interacting with experienced entrepreneurs. He traveled to Silicon Valley and many other places, but it is San Diego, where he built his network of advisers and supporters. Both Low and Krishnan have built their own companies and teams by capitalizing on experience and expertise of seasoned entrepreneurs instead of participating in any firmly established community from the beginning. However, they can access knowledge and practices, which have developed in many communities.

While Krishnan and Low run their first companies, John Stuelpnagel is involved in building his second start-up after leaving his first company, Illumina, which he cofounded in 1998. By contrast to Krishnan and Low, Stuelpnagel began to develop his skills and business practices by working with Larry Bock, a partner of Avalon Ventures. During his second year at an MBA program, he had an internship opportunity of working at Avalon Medical Partners – founded by Kevin Kinsella – where he met Larry Bock. Stuelpnagel learned the practice of Avalon Medical Partners by observing and assisting Larry Bock. Stuelpnagel (interview) said of his learning experience: "I was able to gain this experience because what Larry was doing was exactly the kind of things I wanted to do."

Managing a venture funding of Avalon Medical Partners, Stuelpnagel and Bock ran across a gene analysis technology developed by a scientist at a research university (David Walk at Tufts University). They met the scientist and did due-diligence by surveying the genetic analysis technology and its market landscape. They concluded that the technology was "something that was going to change the way people do" genetic analysis. Stuelpnagel described their actions for founding a start-up in 1997:

> Larry Bock let me run with it. So, I licensed the technology, became the acting president, CEO of the company and started to build a management team. (interview)

In 1998, he hired an employee and started to raise a series of venture funds. When the company, Illumina, went public in 2000, it was valued at more than one billion dollars. (In large part it was due to the public frenzy toward the human genome project in the year.) During the same year, a seasoned executive came in as a CEO and Stuelpnagel took responsibility of business development for two years and then operations for six years.

He led Illumina’s efforts to develop and manufacture products. He took charge of developing corporate partnerships, addressing patent litigations and building manufacturing facilities. These experiences at Illumina let him learn about building and running a company, as he (interview) said: "I learned through all of the process, absorbing lots of inputs including Larry Bock and scientists and lawyers who I worked with." He likened the process as "learning by hard knocks." In the process of dealing many business issues, he developed skills and practices for running biotechnology companies: (1) he became an expert in licensing in virtue of his negotiating experience with a research university (This experience was utilized in licensing a technology from TSRI to create his second start-up.); (2) he spearheaded his capacity for developing corporate partnerships through his experience in building strategic alliances; (3) he developed deep understanding on issues related to intellectual property by "having run an intellectual property team and having worked with dozens of IP [intellectual property] attorneys" at Illumina; (4) he learned how to manage R&D, operations and manufacturing (interview).

In addition to practices at Illumina, interactions with many 'entrepreneurial managers' (in words of Stuelpnagel) in San Diego have been another source for learning. In the process of running Illumina, he was able to interact with many entrepreneurial managers: "just being at Illumina, I met a lot of them, because there're lots of people coming to us to propose partnerships and I would reach out and propose partnerships to others" (interview). The local trade associations including CONNECT and BIOCOM have provided another opportunity to network with many entrepreneurs. As he succeeded in developing products and expanding the company, he became known as a successful entrepreneur. He has been approached by young entrepreneurs who want to access his knowledge:

> I got approaches by a lot of young entrepreneurs, and occasionally helped some. I enjoy. That's part of what I do today: I help young entrepreneurs. I help them on their strategies; I help them in their financings; and sometimes in the case of some new companies, I roll over my sleeves and get dirty with them. (interview)

Stuelpnagel attributed the development of San Diego biotechnology cluster to the existence of a community of “entrepreneurial managers”, who are able and willing to help newcomers as well as experienced entrepreneurs. Stuelpnagel began his entrepreneurial career by participating in Avalon Medical Partners, and he, in conjunction with Larry Bock, established Illumina on a basis of Avalon Business Model. He developed his expertise and practices to be a skillful entrepreneur through dealing with issues at Illumina and interacting with partners and “entrepreneurial managers.”

Like Stuelpnagel, Paul Laikind, cofounder of three companies – Gensia Pharmaceuticals (1986), Viagene (1987) and Metabasis Therapeutics (1999) – and chief business officer and senior vice president of business development at the Sanford-Burnham Institute, has developed his entrepreneurial capacity and identity through being involved in the biotechnology business and interacting with many peers and partners. After completing his Ph.D. study in chemistry, he continued at UCSD as a postdoctoral researcher. There, among other projects, he did research on metabolism related to autism in the early 1980s. He published some of the early work he was doing on the disease, and it was also featured in a local news media segment, which caught the eyes of a local lawyer. The lawyer, having a son with autism, visited the research team to learn about their research project and became a supporter. Eventually, after noting that the research team was devoting a large part of their time to writing grant proposals, the lawyer proposed that Laikind and his associate, Harry Gruber, consider starting a company. Laikind and Gruber entered into the biotechnology business with the encouragement of the lawyer:

> Frankly, neither of us had any real concept of starting up a company. But we did have a technology which we had been working on, and actually talked to some potential corporate partners about. So, we said yes. (interview)

The lawyer brought together a group of angel investors who provided the seed funding of approximately $100 thousand. Laikind left UCSD and founded Gensia Pharmaceuticals in 1986 with Harry Gruber as co-founder remaining at the university initially to manage the science. Soon after, as he said, "we were able to get the top name venture capitalists involved and get the company up and running in reality" (interview). At "school of hard knocks," he said, "I was a scientist with no business training. I had a lot to learn and didn't have much time to do it." He gave an example illustrating how he had to climb a steep learning curve to understand the business aspect of science. When he started Gensia Pharmaceuticals, a venture capitalist who had invested in the company asked him to produce a budget plan. At that point, he had no idea about corporate budgets and there were only an administrative assistant and a technician at the company. He immediately called a chief financial official of a one of the venture capital firms, that were participating in the funding round, saying "help, I don't know how to do it." The chief financial official asked him to organize and send ideas, data and projections to him, so that he would construct a spreadsheet for budgeting and projecting. Laikind described what followed:

> I worked with some local entrepreneurs in town. They helped me think through some of strategies and such. So, I did that. I sent it to him, he sent back a very nice spreadsheet with all the data in it. Of course, when I got it back, I realized I needed to change a bunch of things. But I had no idea of how to change it, how all the various items are related to each other. What I did was I printed the excel worksheet out in such a way that it showed all the formulas. I printed out the entire spread sheet with formulas. And I studied it to figure out how everything was related to one another. That allowed me to modify the budget and the forecast. (interview)

Learning through experience "takes perseverance and willingness to work hard," he said. To learn through experience requires, most of all, a positive attitude and persistence, as Laikind (interview) pointed out: "you have to have a very positive and optimistic outlook, and you should be willing to work very hard: I hardly took a vacation for the first five years at Gensia." In addition to learning through trial and error, the other part of learning came in the process of interacting with co-workers and advisers: "the goal is to always surround yourself with best and brightest people, then you observe and learn from them. This exposes you to the best ideas and helps build your own skill sets." He learned from the people he worked with including associates, investors, accountants, lawyers and advisers. Now, he applies the experience of business development and business running to turning research discoveries at the Sanford-Burnham Institute into products and companies.

David Kabakoff, who joined Hybritech as a director of its R&D division on diagnostics, exemplifies the translational process from a scientist into a veteran entrepreneur. He takes charge of the local office of a Silicon-based venture capital firm, Sofinnova Venture Capital. In 1976, he entered into the biotechnology industry with a Ph.D. in chemistry, and in 1983 he came to San Diego to lead Hybritech's diagnostic R&D division. His career at Hybritech, several start-ups and a venture capital firm spans his learning pathway from a laboratory scientist into a skillful, seasoned entrepreneur. Along his learning pathway, he has also contributed to creating several companies and educating a cadre of fellow entrepreneurs.

Leading an R&D division at Hybritech, Kabakoff expanded his knowledge and interest beyond the science of chemistry into the drug development and management: "Based on [my R&D] experience [at Hybritech], I was eventually able to move from diagnostic world into drug development and biotechnology world" (interview). As a scientific director, he often engaged with the management team of Hybritech in discussing issues like strategic alliances. The engagement and exposure to the management issues at Hybritech allowed him to develop business savvy. In 1989, he left Hybritech to head a fledgling company, Corvas, which had been founded three years prior by a group of scientists at TSRI. During his tenure at Corvas as president and CEO, he led the start-up's efforts to develop products, conduct clinical trials and create corporate partnerships with large pharmaceutical companies. He recalled the experience:

> The time at Corvas was really when I made the transition from running laboratory science to business management and general management, which I have done since. (interview)

At Corvas, Kabakoff had opportunities to have interactions with a group of venture capitalists, who provided guidance for him and his management team about how to develop and run the company. He credited his current practice as a venture capitalist to these interactions: "That was my first direct exposure to venture capital, which now I am doing."

Prior to becoming a venture capitalist, Kabakoff had been involved in two successful companies. In 1996, he joined Dura Pharmaceuticals, a specialty pharmaceutical company run by Cam Garner, as a senior manager. Soon after the company was acquired in 2000, he co-founded Salmedix with Dennis Carson, director of UCSD Cancer Center, and Wendy Johnson, who joined Salmedix as vice president. After four years, this company was successfully acquired at $200 million by a pharmaceutical company due to its drug candidate for treating cancer. Following the acquisition, he participated in the Executive-In-Residence (EIR) program at CONNECT, where he met and mentored young entrepreneurs. In the process of mentoring and consulting, he helped found a start-up, Trius Therapeutics – a developer of antibiotics. Then, he became a partner of a venture capital firm, Sofinnova Venture Capital, whereby he has engaged with start-up entrepreneurs as an investor, director and mentor. He always encourages young entrepreneurs:

> There have been a number of very successful companies here. There've also been companies that have failed to achieve their goal. But I tell people that companies and projects may fail, but good people don't fail. They learn something from every experience. They take it with them, and they do the next new thing. (interview)

One of the companies in which Kabakoff invested and engaged is Intellikine. Intellikine was cofounded and run by Troy Wilson. The experience of Wilson shows how a young entrepreneur becomes engaged with and benefits from interactions with seasoned entrepreneurs. In accounting for his own learning experience, Wilson referred to Kabakoff as his mentor:

> I'm very fortunate, for example, [in that] on my board we have David Kabakoff. David is my mentor. I talk with David frequently about what we're doing, what

> we're planning, and David would help guide me, and suggest what we might do, or might not do because David has done it. He has the experience. (interview)

According to Wilson, the way to learn skills and gain insights is to work with people who have done it before. And it is companies where he has surrounded himself with these seasoned professionals.

Similar to Kabakoff, Wilson leveraged his on-job practices to transform himself from a scientist, to a legal practitioner into, finally, an experienced entrepreneur. After completing his Ph.D. in chemistry, he entered law school and then worked for an internet company as an attorney. Wilson first came to San Diego in 1998 to lead legal and licensing functions at Novartis Institute for Functional Genomics – (later renamed GNF) an R&D arm of Novartis, a Switzerland-based pharmaceutical company. At the Novartis Institute, he overviewed the licensing functions and business development, which involved "agreement drafting, negotiating and understanding what scientists need, how to put them into projects and how to make legal agreements" (interview). The experience on the job was part of his learning curve. He recalled, “I learned a lot on the job at the first two or three years, and that was how I got started." He attributed his attainment of skills to the complexities of job practices:

> [GNF] was a wonderful environment with creativity, initiative and energy. It was just a very exciting place to be. It was also very complicated because all of those relationships had to be managed from legal and business standpoints. It was complex and moving quickly. (interview)

After working a couple of years practicing licensing and negotiating, in 2001, he led the institute's efforts to create start-ups that would commercialize research discoveries. The efforts to attract venture capital and construct companies led to spawning three start-ups. He referred to the experience as his second turning point of his career pathway:

> That was where my focus began to change and my skills became more sophisticated because now I had to not only focus on making sure that the science was supported, but I had to get these companies started by recruiting management teams, attracting venture capital and setting up independently operating businesses. (interview)

The experience of creating companies gave him the ability, confidence and inclination to run a company on his own: "I was ready to try and to be more entrepreneurial myself, rather than just starting companies and letting someone else be responsible." Wilson left the Novartis Institute to become the first employee of a new start-up, Ambrx, in 2003, and ran the company as CEO until 2007. As he stated in an interview, this on-job experience "gave me a great experience because that was the first time that I had the opportunity to work with a board and venture capitalists, to recruit a team of people and to do corporate partnerships." He remembered this period as the third and final mark in his career to be an entrepreneur who "really looks at these companies less as a scientist and much more as a business person." He left Ambrx to be a founding CEO of Intellikine in 2007. With each company, he said, "I got better and better." With more experience, he has become more "sophisticated in understanding about what not to do," and able to see the bigger picture.

One of the senior managers with whom David Kabakoff founded and ran Salmedix is Wendy Johnson. She joined the company as the first employee and remained with the company as a vice president of business development and strategy. At the company, she led the company's effort to license in a cancer treating compound which had already been used in Germany for 30 years. This compound, following its completion of the Phase II clinical trial, was sold to a large pharmaceutical company at $200 million, which was acclaimed as one of the most notable successes in the San Diego biotechnology community. Johnson came across the compound by accidentally while reading a journal article and searched all the literature because she was interested in it. She kept reading the publications on clinical trials of the compound by German physicians. Attracted by the potential of the compound, she went to Germany:

> I went around and spent months in Germany talking to the doctors who used the drug. By the time, I was done, I was convinced there were something of value that people never recognized. (interview)

The compound led to an acquisition, which was such a bonanza, particularly, to the company's investors that several venture capital firms asked her to join them to redo the process – discovering a compound, licensing in by establishing a start-up and developing in clinical trials – saying "you are really good at it, and restart it again as you did for that company," as she put it. She joined one of the venture capital firms and soon launched two start-ups – Aires Pharmaceuticals and Palkion – based on the business model which she had put into practice at Salmedix and the financial model which the venture capital firm had been practicing. To her, "it was once in a lifetime," a consequence of a life-long learning process.

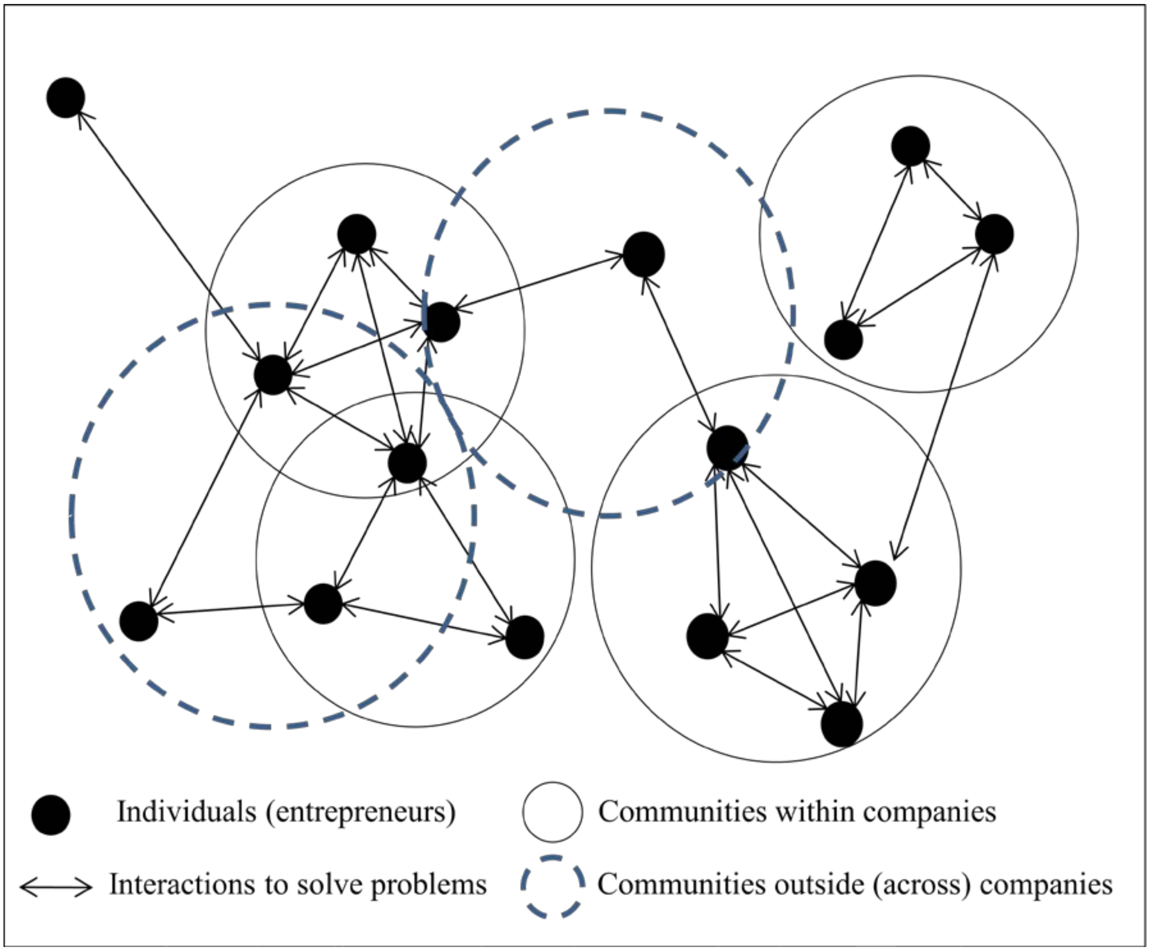
Johnson had to move across many start-up companies and learn from trial and error to be able to identify promising drug compounds and to execute licensing deals. She started her career running a laboratory at a hospital as a trained clinical microbiologist for a year. Then, she found her next job at the FDA as a reviewer of applications and stayed there for ten years managing an extramural research program and dealing with regulatory affairs. Finishing an MBA degree which she had entered in the hope of learning more about business, she started her first industry career at a biotechnology company in England. At the company, she was involved in market research and regulatory practice, which gave her opportunities to meet experts and to understand the industry. In 1988, she moved to San Diego to look for a new job in 1988 because the company was in a financial problem. It turned out that she had to switch from job to job at a number of biotechnology companies every a few years because each of them ended in failure. At these companies, she was mostly involved in discovering and licensing in drug candidates as either a senior manager or an outside consultant. Johnson recalled her experience at one of these start-ups, which was her second employer in San Diego:

> I got an opportunity in four years to travel all over the world to visit almost every pharmaceutical company in the world and to start to make contracts: a couple of deals in Japan, several in Europe and a few in the U.S. That's really how I got my business development experience. (interview)

As the company failed on the way, she moved to three more companies, where she led efforts to identify, negotiate and bring in drug compounds.

All of these cases from Krishnan to Johnson depict that individuals become entrepreneurs through acting and interacting in communities for learning and practicing. Figure 5-3 represents where and how individuals develop their skills and identity by constituting or locating themselves in communities. The circles indicate communities, in which participants “share a concern, a set of problems, or a passion about a topic” and develop their knowledge and expertise “in this area by interacting on an ongoing basis" (Wenger, McDermott & Snyder, 2002, p. 4). The dots outside the circles depict newcomers or independent entrepreneurs not yet belonging to any company-based communities of practice. The dashed circles in Figure 5-3 indicate discussion groups or forums which are constituted to solve certain problems by collectively developing strategies and relationships. As the cases of Krishnan and Low tell, many entrepreneurs belong to these communities outside their workplace. Krishnan met two advisers of the von Liebig Center, and they have kept interactions on an ongoing basis. The Springboard program at CONNECT constitutes a group of experts to coach and guide for a young entrepreneur. If the young entrepreneur keeps interactions and develops deeper relationships with some of the experts in the process of addressing many issues together, they constitute a community for learning and they accelerate their learning process. Many of the participants keep their relationships and interactions even after they achieve their goals and officially disband their group. Overall, communities are constructed in the process of solving problems in collaboration. Some communities last for decades, but some of them go for a short time. A managing team or a group of scientists at a single company can constitute a community for learning and supporting, but individuals from multiple companies or professions can keep robust interactions to deal with shared issues for a certain time span. In any cases, communities enable their participants to develop their knowledge and practices in the process of taking actions and interacting with other participants.

**Figure 5-3.** Developing knowledge and practices in communities




Individuals learn to be entrepreneurs through practicing and interacting in their communities. Not every start-up was established by skilled entrepreneurs, but every start-up grew to be significant and sustainable by a band of skillful practitioners. The scale and speed of entrepreneurial activity have resulted from the development and deployment of the knowledge, practices and entrepreneurial culture of the San Diego biotechnology community. The momentum of the San Diego biotechnology cluster came from its advantage of cultivating entrepreneurship through robust interactions in and across communities. Some entrepreneurs learned to be skillful by utilizing their job experience at multiple companies and in multiple networks. Other came from outside San Diego, attracted by its opportunities and openness. As a geographically and historically isolated community, entrepreneurs and local leaders also constructed collective memories and practices based on frequent encounters and interactions. Leadership, especially by William Otterson and trade associations, led by CONNECT, created the framework for celebrating entrepreneurial achievements, encouraging openness and emphasizing collaborations. The shared understanding and identity have helped lower the boundary between communities, which have extended the learning opportunity across communities of practice, and facilitated the creations of many communities for learning.

Therefore, the first factor which contributed to creating the San Diego cluster was a critical mass of entrepreneurs and employees, and their learning experience in communities, which often overlap small start-up companies. It was not only Johnson who had to move from company to company, but most entrepreneurs and professional practitioners have experienced job-to-job movements across companies. The experience, as Denise Lew (interview), who had worked at three companies before landing on the Technology Transfer Office at UCSD, put, "is difficult for people to find their next position, but it forces them to be very creative in what they want to do next or in what they look for in their job search."

Historically, the biotechnology industry in San Diego has been composed of a mass of small start-up companies that are vulnerable to any negative impacts because of their limited base of resources and capabilities. During an economic downturn or individual firms' failure to achieve their milestones, many of these small companies had difficulties in raising funding, and had to end their development program. Although they succeeded in testing drugs in the later clinical trials or in gaining the FDA approval, in most cases, they chose to sell their product or company to large pharmaceutical companies since they lacked the experience and expertise to bring their drugs to markets. To employees, it means they have always been exposed to the risks of layoffs.

Lew described the collective experience of many employees in the local biotechnology industry:

> What happened in a place like San Diego was there were a lot of startup companies. Many people have been forced out of the companies that they have been with whether because it was an economic downturn or simply because new management had come in and they no long wanted to pursue the particular path… It's really amazing how many companies have come and gone since then. But at least people gave a try. I have friends who have worked at various jobs one after another at small companies for a year or two, and then found themselves laid off. But each time they acquired more skills and more experience by working at startup companies. And now they feel at this point that they have learned enough about the startup companies and where the pitfalls are when they start up their own companies. People go through these experiences and these experiences are forces upon them, therefore became an important part of what developed new companies. (interview)

The exodus of Hybritech employees was the first and most significant event which freed a breed of young, highly motivated entrepreneurs. As David Kabakoff (interview) pointed out, the acquisitions of several successful local companies by large outside pharmaceutical firms forced their employees, particularly senior managers, to redo start-up activity; the acquisition of Agouron Pharmaceuticals which had developed an AIDS treatment, Viracept, by Warner-Lambert in 1999, which was again acquired by Pfizer in

2000; Dura Pharmaceuticals by Elan in 2000; the 2003 Biogen-IDEC merge. Along with the large-scale acquisitions, there have been countless acquisitions as a result of either success or failure.

However, not only employees at dissolved companies have been forced to be independent; many people at companies in operation have chosen to put their own skills and luck into experiment. Julia Brown, an angel investor, observed this phenomenon as:

> If [employees] see the opportunities to become entrepreneurs, some of them step out on their own and try to do that. Sometimes, they leave a successful company because there is already a CEO but they want to be a CEO. Other times, when the company was sold or has failed, they decide to start one instead of taking a job at another company. (interview)

Second, a part of knowledge and practices has come from outside as many seasoned entrepreneurs were recruited by companies in San Diego. Groups of entrepreneurs and executives who had been trained at large pharmaceutical companies as well as biotechnology companies outside San Diego have flowed into San Diego through various routes. Since San Diego had no tradition of the pharmaceutical industry, a large of portion of management talent, competent with regulatory process and manufacturing and commercial activity – marketing, sales and distribution, had to be brought in from outside. Many of them were scouted by companies in San Diego to expand their capacities into late-stage development activity. The formation of Hybritech's management team in the early years is an illuminating case: virtually all senior managers came from outside San Diego. There is also a group of people who came to San Diego lured by its rich amenity for start-up activity. Another route in which talent arrived to San Diego was the acquisitions of local companies and the subsequent establishments of local facilities by large pharmaceutical companies based on acquired local firms. Ivor Royston (2002) noted about this talent group:

> With the arrival of large pharmaceutical corporations came seasoned biotech management that can be recruited to work at start-ups, teaming up with scientists to launch companies, guide them through their development and take them through to IPO or acquisition.

The acquisition of Hybritech by Eli Lilly brought Eli Lilly's senior executives, who were capable of dealing with pharmaceutical business, into San Diego. The CEO of the Hybritech division, Donald Grimm, retired from Eli Lilly in 1993 and joined a local company, Telios Pharmaceuticals. Julia Brown, who took charge of worldwide marketing for the acquired Hybritech, chose to stay in San Diego to participate in a number of start-ups and community initiatives instead of returning to Indianapolis.

The skill set and expertise of individuals having training at pharmaceutical companies are, in many ways, complementary to those at small companies. Most activity at start-ups is limited to early-stage processes, so the on-job experience could not be the basis for proceeding with late-stage process. In contrast, employees at large pharmaceutical companies are exposed to more diverse, sophisticated processes. Jack Florio, who had come to San Diego after retiring from Eli Lilly, said of his contribution to San Diego:

> In my career in Eli Lilly, process was extremely important. We had processes for most business functions and activities. These processes, while they tried to insure a higher quality, many times slowed our actions and reaction time. On the other hand, small companies here have little or no process. Folks coming out of big [pharmaceutical companies] can provide value by helping put in place some of the processes that [small companies] need. (interview)

In addition to their versatility at dealing with complex processes, they can develop a broader spectrum of skills and perspectives through engaging in more diversified activities. Large pharmaceutical companies, noted by Julia Brown (interview), put emphasis on developing talent "using job rotation, so they would move you from one kind of assignment to another with a specific objective of having you learn things and develop new skills and different perspectives," which is not feasible at small companies since at small companies, it is more individual's responsibility and initiative to develop one's own capacity. In sum, the talent, come from outside San Diego, broadened the spectrum of experience and expertise in San Diego by participating in many communities of practice.

Third, the leadership, organization and culture of the entire San Diego community have been another key to facilitating the learning process of its members. Whether individuals have become either a veteran entrepreneur through a long-term engagement in their communities or they have arrived from outside equipped with sophisticated craft, it is engagements and exposures at the local community that have helped nurture, reshape and update their ability and identity. The accessibility and availability of the repositories of knowledge, practices and culture is crucial, in particular, to newcomers who have not yet sufficiently developed skills, ties and memberships with any ongoing communities. The interactions and interchanges with old-timers have been the most critical venue for new entrants to learn by accessing stocks of knowledge created and enacted in established communities. The regional advantage of San Diego is, most of all, the presence of seasoned entrepreneurs willing to mingle with newcomers and a culture of collaboration, as Julia Brown (interview) said:

> There are a tremendous number of people in town who will work with entrepreneurs to show them the roads, and help them see what they need to do: just give them advice. They contribute not only financially, but also contribute their experience and wisdom, and help the entrepreneurs understand what needs to be done, which sources to use, how to refine the business model, how to make their presentations and what to do to get funding.

The interactions are 'a two-way street' whereby seasoned entrepreneurs identify new opportunities and talent, while young entrepreneurs gain knowledge necessary to take entrepreneurial steps. Furthermore, every participant develops his skills and expertise in the process of seeking to find or invent solutions for ongoing problems together. Discussion and conversation do not only transfer knowledge between participants, but also help every participant develop new knowledge. An entrepreneur stated: “I advise based on my own personal experience and also based on what I discussed with other people in the biotechnology industry” (Ryan Bethencourt, interview). Duane Roth, CEO of CONNECT, described the benefit of participating in teamwork to solve problems:

> It is clear that to give back idea and share your information is really important. They [participants of CONNEC programs] get a lot of networking, exposure and learning opportunities… What I have learned is the more I share, the more I get to know from others at their expertise. Let's say there is a Springboard company that has a problem, and that is trying to solve [the problem]. Maybe there are a half-dozen or a dozen people in the room, each with different experiences that can contribute to solving that problem. The more they work together to help solve the problem, the more they get to consensus about what should be done. (interview)

The interactions between individuals from different communities happen and produce benefits when they stand on a shared ground of experience and enterprise. Experience and artifacts in common allow participants to interpret and embody narratives in guides for actions as well as encourage them to engage in interactions. David Kabakoff articulated his experience:

> I think you should have a lot of common business experience and sharing business experience just because the way the community grew up. And if I have a business problem or a question, there are a lot of people I can call. Generally I get some good advice from colleagues and vice versa. (interview)

The local community of entrepreneurs has produced, activated and disseminated communal meanings in forms of narratives, artifacts and iconic figures. CONNECT, under the leadership of its founding director, William Otterson, created a sense of community and has been the repository and activator of shared meanings. Because most entrepreneurs benefitted from programs and advocacy of CONNECT and Otterson during the 1980s, many of them would like to make contributions to the community. David Kabakoff said of his motivation of serving the community:

> In my case, my companies and personally I benefitted a lot from CONNECT. Especially, in the very early days of Corvas when the community wasn't as large as it is today, and it wasn't as strong, we really did benefit from that association… I wanted to take some time off to be involved with the community. (interview)

CONNECT is recognized, mostly, for its role of resourcing but, more importantly, it has been a platform for organizing talent to facilitate the learning process at the entire community level. Mary Walshok accounted for the role of CONNECT:

> If you look at CONNECT's programs, you see how everybody who participates in the ecosystem. It's always learning new things. There is much more shared knowledge about new economy strategies, opportunities and challenges, and lots of trust and familiarity. What we call in sociology 'pre-transactional relationship'. Lots of scientists know attorneys, accountants, and lots of marketing people know chemists and biologists before they do a deal together and they ever work together

> officially to grow a company. And I think that is the secret of CONNECT. (interview)

CONNECT provides the space and creates the cause where many volunteers can settle down. Every year, CONNECT organizes events and initiatives that celebrate the efforts and endeavors of local entrepreneurs by convening the entire local community, to which Duane Roth (2008) referred as "a bunch of events networking, recognizing and connecting people."

Besides CONNECT, BIOCOM has been another nexus of interactions, as Joseph Panetta, CEO of BIOCOM, said:

> We provide networking opportunities for them to get to meet people who might be experts. We have about 100 different events a year: We have roundtable discussions with CFOs, we have CEO receptions. Most important thing for CEOs we have is every month we do a mentoring gather, where we have experienced CEOs and about 15 less experienced new CEOs. The conversation between the experienced CEO and newer CEOs gives new CEOs the opportunity to learn from the mentor. We have lots of different breakfast meetings and committees. (interview)

Like CONNECT and BIOCOM, organizations including the San Diego Tech Coast Angels, the CleanTECH San Diego and the San Diego Venture Group have been another channel for engagements, interactions and participations. Along with the learning experience at companies, these organizations and their programs have helped create a social space for convening and conversing, which have promoted cross-fertilization of knowledge and practices between communities of entrepreneurs.

While a number of individuals have transformed into seasoned entrepreneurs by engaging with communities, many them have developed their expertise and practices to be investors and specialized service providers. These specialized practitioners constitute a significant part of economic activity, and they are involved with entrepreneurs in solving problems at various situations. Since small and start-up companies comprise the majority of local population, the depth and breadth of specialized practices is a key to building and expanding their enterprise. Indeed, entrepreneurs have to tackle shared issues like regulations on building and recruitments of skilled employees. The following section looks at how investments and specialized services have developed and how the local community has built a culture of collaboration.

## 5-4. Creation of Resources by Learning and Practicing

### *5-4-1. Venture Capital Firms and Angel Investors*

There is not a strong community of venture capitalists in San Diego. From the beginning, most local start-ups drew on Silicon Valley and the East Coast for venture capital funding and expertise. Only a few venture capital firms focusing on life sciences have emerged locally. One such local venture capitalist is Kevin Kinsella, who founded Avalon Ventures in 1983. In 1986, Biovest Partners was formed by two Hybritech senior managers, Howard Greene and Timothy Wollaeger investing in six start-ups with its first six million funding, but it disbanded in 1989. In 1993, Ivor Royston, founder of Hybritech, started Forward Ventures with a partner, Standish Fleming. Enterprise Partners, founded in 1985, moved its headquarters to La Jolla from Newport Beach in Orange County in 1999. The scale and vibrancy of San Diego-based venture capital funding is not comparable to the biotechnology hubs like Silicon Valley and Route 128, so its biotechnology industry had to reach out venture capital firms outside San Diego from the beginning.

Several venture capital firms located outside San Diego established their local office to have more interactions with the local community during the early 2000s. Among these firms, Domain Associates from New Jersey built a local foothold in 2006 and Sofinnova Ventures also established a local office (Crabtree, 2006c). Both of them recruited local entrepreneurs, Eckard Weber and David Kabakoff, as the managing partner of the San Diego offices, respectively. Although the local venture capital firms and offices of outside firms have been pivotal to fueling capital, a large part of funding and services have come from Silicon Valley-based venture capital firms, about which Scott Forrest (interview) said: "had San Francisco not been there, there would be a lot of troubles." In contrast to San Diego, San Francisco has been the center of venture capital by virtue of its strong and relatively long tradition of high-technology and financial industries. Scott Forrest (interview) attributed the weakness of venture capital compared to other sectors to the lack of late-stage activity by stating San Diego "is much more research oriented" while "San Francisco has older companies, commercial stage companies with products in the market, market expertise and more on." In addition, San Diego has not developed financial industries to a significant level, which restrained the development of financial expertise and tradition. Therefore, without a sufficient pool of talent experienced at activities on both sides – a long tradition of technology-based industries and financing institutions – San Diego has not failed to develop its own venture capital practice to a full extent.

In contrast, the region has cultivated a vibrant community of angel investors, who invest their own capital in start-ups. The number of angel investors and their activity in San Diego are prominent even in the national landscape. In the late 1990s, about 20 wealthy individuals, mostly having experiences in management, formed a network, the San Diego Band of Angels, patterned after the first angel group in Silicon Valley, the Band of Angels. It was renamed the San Diego Tech Coast Angels in 2000 when it merged with an angel network group in Orange County (the Tech Coast Angels of Orange County) (Bigelow, 2000).

But until the early 2000s, there was virtually no deal in the area of life sciences. The majority of its members had background in high-technology industries, so they could not evaluate business plans and the involved risks in the life sciences sector. As Jack Florio (interview), vice president of marketing and communication at the San Diego Tech Coast Angels, said, "part of the problem in the past was that when the life science deals came into the group, which was composed or primarily individuals with a high tech background, they had no understanding of the science or the technology, and therefore no way of evaluating them; there were significant differences between tech and life science deals." Furthermore, while technology-based businesses were less ambiguous and took relatively short time for reaping investments, the complexity and time-span involved in developing health-related products kept angel investors from venturing into them.

A few members including Michael Lutz, a high-technology entrepreneur, and Donald Grimm, a former Eli Lilly's Hybritech CEO, sought ways to invest in life sciences businesses. According to Jay Kunin (interview), a vice president of BioMedTrack at the San Diego Tech Coast Angels, they thought in this way:

> San Diego is a fairly active biotechnology town but the Tech Coast Angels have focused on mainly high-tech deals. So, why don't we get a startup program trying to find deals and new members from that space?

They brought in a few individuals who either had background or an interest in biomedical industry. Among the participants were Jay Kunin and Jack Florio, and soon they formed a committee, BioMedTrack, in 2002. The founding members of BioMedTrack started, in words of Jack Florio (interview), "to sort out how to bring life sciences deals into the Tech Coast Angels, so they could be evaluated by both investors in high tech companies as well as life science companies." They worked to build practices, processes and programs to educate them as well as to evaluate life sciences deals. The participants, led by Michael Lutz, structured prescreening meetings whereby they discussed issues about life sciences businesses in conjunction with outside experts from various professions. They inaugurated a seminar series where experts were invited to give lectures.

Out of these efforts, the BioMedTrak team incrementally developed expertise and practices to screen life sciences business plans. In the words of Jack Florio (interview), "we started to ask a lot of these questions and over time we were able to tell the deals we were bringing in differently." Along the way, they gained more traction from members of the network group, as they could explain the elements of life science business. As Jack Florio said, "we got some tech guys who wanted to get involved in life science prescreening teams because this was a great opportunity for them to get educated." Ralph

Mayer (interview), a president of the angel network, who had initially no "knowledge on life sciences at all" told what happened as a consequence of involvement:

> A period of about two or three years, we got to the point about a third of our members had life science backgrounds. And there were a fair number of others who even didn't have the knowledge background, but learned enough to start to evaluate investments.

To date, the San Diego group is considered to have the best expertise in life sciences among the five local chapters and life sciences account for about one-third of their total deals according to Jay Kunin (interview).

Besides educational programs, the BioMedTrack group in conjunction with the Tech Coast Angels instituted a process to screen and evaluate business plans, and to present the final proposals to the entire network groups. To raise angel funding, typically each applicant goes through a set of procedures. The first step is a prescreening whereby a team from the BioMedTrack group reviews an application, frequently, by having face-to-face talks with the applicant. If the applicant passes the prescreening, it pitches its business plan to a group of BioMedTrack members at a screening meeting. Successfully completing this phase, the company enters into the due-diligence process. A new due-diligence team consults with outside experts to reasonably evaluate the odds of success. After this process, at a monthly dinner meeting, the deal leader who headed the due-diligence process introduces the company to the members of local chapter, and then he repeats this process at the other four regional networks.

Education occurs in the process of engaging with peer groups to address any arising issues, as Jack Florio described:

> The people in the [prescreening team] all have background in life sciences… So, there is a lot of different expertise around table. So, we do the prescreening with some level of knowledge by helping each other… If you get on a due diligence team, and you are sitting there with a bunch of people talking about the technology, the issues about management, the issues about regulatory path and so on, so you learn from being actively involved.

In addition, the angel network provides formalized training programs to their members, which include a full-day course about how to be an angel investor and a series of seminars every year. The training programs, according to Ralph Mayer (interview), teach its members "what you need to be an angel investor: what the term sheet looks like, which should be done during due diligence, what you should look for in patent searches and IP (intellectual property) protection." As entrepreneurs in San Diego have learned to be familiar, comfortable and capable with biotechnology business through engaging in communities, angel investors have developed expertise by participating in the practices and process of screening, evaluating and presenting start-up businesses. It was the organization – both the San Diego Tech Coast Angels and the BioMedTrack group – that has cultivated the local stock of knowledge and the set of practices for angel investments.

Further, the angel network has grown to be a significant constituency of the local community of entrepreneurs. In addition to producing and providing a platform for activating resources by promoting learning and interacting process, it has attracted a number of seasoned professionals to San Diego and enabled or encouraged them to participate in activity like learning, mentoring and investing. Regarding the participations of its members in the community, Jay Kunin (interview) described it this way:

> We are very well connected in the community… There are the guys who don't spend their time on the golf course, so they want to be involved in start-up

> companies. They are all involved in the community in one way or another whatever their interests are.

The members of the San Diego Tech Coast Angels comprise a core part of the CONNECT Springboard Entrepreneurs-in-Residence, who help the novices launch and steer start-ups. Another contribution to "creating a vibrant entrepreneurial community," as Ralph Mayer (interview) said, is its annual business plan competition, called Quick-Pitch contest. He (interview) pointed out that the competition "provides a vehicle for entrepreneurs to get in front of potential investors and partners," so the young entrepreneurs can gain visibility and credibility. Overall, the organization and activity of the network group have been critical in helping newcomers, both as angel investors and guides.

### *5-4-2.Specialized Services: Legal and PR Practitioners*

The emergence of specialized service providers in San Diego including intellectual property attorneys, public relations practitioners and real estate developers is attributable to the growth of local talent having the expertise and practices to help entrepreneurs deal with many problems. As the biotechnology industry in San Diego started to grow from the late 1980s, local legal firms responded to seize the market opportunity by developing their specialty in biotechnology, and, at the same time, companies from in Silicon Valley and the East Coast started to establish their local office (Dower, 1988). Law firms in San Diego began to develop legal practice for the biotechnology industry by creating new divisions or recruiting local practitioners, but none of these have risen to be a major player in the national landscape. Similar to the venture capital sector, the core part of legal expertise has been provided by local offices of large law firms having headquarters outside San Diego, which established their foothold during the early 2000s, primarily lured by the growth of local biotechnology cluster.

Even though the nationally prominent law firms had a large base of expertise and practices, they had to recruit local experts with local knowledge and network (Bigelow, 2004). The importance of a locally developed pool of practitioners is found in an account by John Gartman, an attorney and managing partner at Fish & Richardson's San Diego office:

> I used to work in Silicon Valley, and what works in New York or Austin will not work in Silicon Valley. You need to find a nucleus of lawyers where you hope to open an office, well-connected in the community, with a good client base and good lawyers (Webb, 2005).

A legal recruiter, Larry Watanabe, who is a partner at Watababe Nason & Seltzer, pointed out that there were only 35 partner-level attorneys in San Diego who were practicing in the biotechnology area by 2005 (Webb, 2005). Accordingly, the law firms which sought to establish their local offices in San Diego competed with each other to tap into the local talent pool. An intellectual property lawyer, John Gartman, said about the situation:

> It’s been increasing over the last four to five years. I get calls from headhunters every day from other national firms. They want to break into the IP market here. They want to come in with a critical mass and open an office around an existing profitable and high-profile nucleus of lawyers. (Webb, 2005)

In this regard, the growth of legal practice has been contingent on the quantity and quality of legal experts who are the repositories of local knowledge and practices.

This is also the case for public relations practitioners. The profession requires not only general knowledge of public relations, but also long-time experience and engagement with the local community. A partner of a local advertising firm, Stephen Harrison, said of the necessity of maintaining long-term, intimate interactions with customers: "we have a long relationship with Stratagene (a firm founded in 1985 as a producer of research tools for genetic engineering), which is important in this industry in terms of our ability to effectively understand and communicate the science, which I think we do in original, graphic ways" (Ashmore, 1999). Mentus Inc. was one of a few public relations firms that grew locally by collaborating with biotechnology companies. One of its earliest customers was Hybritech, for which it helped find consultants and do public relations (Howanietz, 1989). Tom Gable, founding CEO of GablePR, started to develop his public relations practice by working with Biovest Partners, a venture capital firm founded by two Hybritech senior managers. Since then, he has developed his profession by interacting with clients and doing research on his own, which he referred to "an ongoing research process to really understand the quality of the company":

> I did a lot of research. I attend a lot of conferences. I participate in local organizations and am always reading and learning, asking the clients whom I work for what are the sources of information that would be helpful for us, and what publications are most important to them. (interview)

In 2006, Porter Novelli, one of the major players in the area, merged Atkins + Associates, a local public relations firm, to tap into individuals having experience and relationships with the local community (Somers, 2006a).

In the end, capital and specialized services, which are regarded as resources, are the product of the learning process through participation and interactions. In the process of doing and interacting, individuals develop their understanding, practices and relationships either as venture capitalists, angel investors, intellectual property attorneys or public relations practitioners.

### *5-4-3. Shaping a Culture of Collaboration*

At the same time, the local community of biotechnology, in partnership with emerging industries, has nurtured a culture of collaboration and a sense of community through a series of partnerships. From the beginning, biotechnology start-ups came across adversities which required collective actions. As the region lacked a significant tradition and experience of life sciences industries, the communities of entrepreneurs had to build large a part of the infrastructure and institutions on their own: they had to explore and enact ways of working with local governments; they had to devise plans and put them into action to overcome difficulties, for example, in attracting venture capital and employing talent.

The first significant issue facing the industry was friction with local governments. In 1991, a group of biotechnology entrepreneurs formed the association BIOCOM, originally named the Biomedical Industry Council, to confront the city's water-rationing program. As much as the biotechnology community lacked the understanding of the political process of the city government, the city also did not understand the needs of the new industry. The early 1990s was a period when dozens of biotechnology companies completed the process of discovery and early clinical trials, so they wanted to install manufacturing facilities beside their R&D facilities on the Torrey Pines Mesa (Fikes, 1992). As a consequence, a series of conflicts and confrontations arose around issues like environment ordinances (the Toxic Free Neighborhoods Ordinance), construction of manufacturing facilities in the Scientific and Research Zone and regulatory process for building permits. And it was also the early 1990s when the city became seriously concerned over the decline of its military-based and real estate industries.

To tackle the demands and threats of the biotechnology industry, the city government introduced several mechanisms to communicate with the industry. First of all, the City of San Diego convened a taskforce team, the San Diego Economic Development Task Force, consisting of a group of business people to identify issues and suggest recommendations (Fikes, 1991c). In 1992, the city designated one of their public officials as a biotechnology ombudsman who would bridge between the public and private sectors (Douglass, 1992). In the same year, the City Council of San Diego held a session, the Biotech Summit, to discuss issues with two associations of biotechnology industry: the Biomedical Industry Council and the BioCommerce Association, which merged to be a single association, BIOCOM (Rose, 1992). As products of these interactions, the city government adopted a set of programs and processes to reflect the demands of biotechnology industry into policies: in 1992, the city took actions to shorten the regulatory review for construction permits and allowed biotechnology companies to build manufacturing facilities in the Scientific and Research Zone under certain conditions (Brydolf, 1992; Fikes, 1992); in 1993, the city led an effort to open a one-stop center, the San Diego Regional Permit Assistance Center, where 14 regulatory agencies convened in one space, to trim down the time for acquiring building permits.

The conflicts between the local government and the biotechnology industry turned into a convergence of interests and initiatives as the result of interactions and involvement. The conflict around the water-rationing plan, for example, was resolved when both sides came to an arrangement in which the biotechnology companies voluntarily would participate in water reclamation and conservation programs and the city would exempt them from mandatory conservation measures. Russell Gibbon, a manager of business development for the City of San Diego, referred to this agreement as an example of mutual understanding and alignment.

> They needed to have a guaranteed water supply. They can't be cut back because water is life blood for biotech. They’ve got to have water for cooling, rinsing, product development, product manufacturing, and all the things. Biotech uses water for so many things. The idea was that if they do the good corporatism of friend by using reclaimed water, and conserving portable water, they won't be subject to any future mandatory cutbacks and conservation measures for the remaining amount of portable water. (interview)

The city needed to understand, as Gibbon (interview) described, "the very specific needs of the biotechnology industry from the policy perspective" and undertake actions to address the needs of the industry. Thus, "a lot of things are about understanding and addressing their concerns from the policy perspective by making sure the city has plans, ordinances and codes."

To the biotechnology community, a core part of its partnership with local governments has been to understand the public sector and build relationships with it. Lynne Parshall, senior vice president of ISIS Pharmaceuticals, in the City of Carlsbad – which is about 20 miles north of La Jolla and is the second largest hub of biotechnology companies in the County of San Diego – explains how the two sides came closer: "We've become more sophisticated. We know and understand the rules, the players, better. We've gotten to know the people in city government more, and know who is the right person to call for this thing or that thing" (Fikes, 1995). As a consequence of interactions and involvement from the 1990s, public and private sides both learned how to collaborate. As Joseph Panetta, CEO of BIOCOM, explained:

> We have also very close relationships with local governments. Sometimes, small companies need to get some approval from the city to build building, to build specialized laboratories or facilities. We work directly with the city and local governments to help these companies get approval. (interview)

Gibbon gave an account from the perspective of the city government:

> We know all the people in these organizations. We know their functions and who their members are because we worked with them [organizations] and individual businesses… Those three organizations [BIOCOM, Industrial Environmental Association and Tech America] and a lot of their individual members constantly contact us, showing up on workshops, showing up in public hearings and presenting to the city council and planning commission. (interview)

From the late 1990s, the biotechnology industry encountered difficulties of recruiting employees. During 1997, the biotechnology industry, for the first time, saw two drugs pass the FDA approval after decades-long efforts: Viracept for treating AIDS, by Agouron Pharmaceuticals; and Rituxan for lymphoma, by IDEC Pharmaceuticals. Subsequently, the companies needed to build full-scale manufacturing plants, which would then need to be filled with employees. In San Diego, the biotechnology industry was in such a rapid course of formation and expansion, that many of them experienced difficulties in recruiting enough employees. IDEC Pharmaceuticals was concerned about the lack of manufacturing workforce in San Diego when it decided to establish a manufacturing plant near its R&D headquarters in La Jolla. In addition, the burgeoning telecommunication and high-technology industries were competing to attract the local skilled labor pool. To address the scarcity of local talent, many companies had to make trips to other states or even foreign countries, but the recruitment and relocation were too costly for most small companies.

To address the issue, people from industry and the public sector adopted two approaches: to develop more talent in their backyard; and to create an environment which would make it easier for local companies to attract talent from outside. This agenda was different from the earlier efforts, which were mainly related to creating partnership with local governments. This was a problem of the entire local community, and it required a variety of approaches. Among multiple approaches were the establishment of a platform for discussion and participation – the San Diego Partnership for the New Economy – and the founding of an MBA program at UCSD. The partnership platform was established in 1998 when "a group of 40 chief executives from a cross-section of the region's premier technology companies assembled" to discuss emerging challenges (SDEDC, 1999). Based on the initial meeting, the San Diego Economic Development Corporation (SDEDC) led efforts to launch the Partnership for the New Economy in 1999 to address issues of workforce development (Lawrence, 2000). In the process, the initial group of 30 industry executives grew to be 300 people from industry, educational and research institutions and local governments. In the end, the group formulated an action plan, titled 'Partnership for the New Economy.'

The action plan called for collaborative initiatives to train talent. The partnership group pointed out the lack of technology industry managers who can build start-ups or grow existing companies. In the action plan, they noted:

> We need a deeper pool of technical and non-technical people who can manage and grow these companies to ensure that San Diego maintains its developing leadership in a range of 21st century industry. (SDEDC, 1999)

To address the issue, the group discovered the need for establishing a management school at UCSD which would train scientific talent to be entrepreneurs. One of the leaders of this initiative, Hank Nordhoff, CEO of Gen-Probe, emphasized the need and potential impact of an MBA program: "We lose them [scientist employees]. They go away, learn about business, and go elsewhere to share their skills" (Beasley-Jones, 2003). Many biotechnology entrepreneurs, along with other industries, participated in establishing a new school, the Rady School of Management, through commitment of funding, teaching and mentoring (Davies, 2004). The school's building was dedicated to William Otterson, the founding director of CONNECT, with its name Otterson Hall. Julia Brown, who was involved in the effort recalled:

> Basically people thought we needed a management school. They thought industries would be better if we had well trained people. So, the Rady School was designed to foster the kind of leaders the emerging industries and San Diego need including life sciences entrepreneurs… Every time I go over there [the Rady School of Management], I read such a wonderful tribute to Bill Otterson in that building that was named for him. Look at how many people in the community contributed to make that possible to honor Bill and what all he did. (interview)

In 1999, the industry group established another platform, the San Diego Regional Workforce Development Roundtable, to enhance communication with educational institutions. Leaders of industries and universities convened at quarterly meetings to ensure the training programs to fit with the demands of regional high-technology and biotechnology industries (Webb, 1999a). These interactions helped open certificate programs at the UCSD Extension, San Diego State University and Cal State San Marcos targeted at developing talent with specified skill sets.

At the same time, the industry people led various efforts to cultivate interest and passion in science for K-12 students. In 1996, a group of 40 business and civil leaders met to find another route to solve the concern over their future workforce. They opened a charter high school, the High Tech High School, focusing on math and science education. One of its founders, Ted Roth, president of Alliance Pharmaceutical, said:

> As products get approved for [biotechnology] companies located here, we'll have a whole new manufacturing infrastructure that will be required… Some of the questions I hear from people is, 'What is high-tech? What is biotech?' 'What are the kinds of jobs [they produce]?' If we could expose 600 kids to that now, that's also families, acquaintances and neighbors that they could tell, 'Here's what they're doing at Lidak Pharmaceuticals; here's what they're doing at Qualcomm. (Siedsma, 1999a)

Several biotechnology companies established a training program or foundation to raise awareness and understanding on sciences. BIOCOM in partnership with the San Diego Workforce Partnership launched the Life Science Summer Institute in 2005, which give high school students and teachers and college students' internship at laboratories. About 30 to 40 life sciences companies have been involved in this program by providing either funding or laboratory positions (Weeks, 2006a). In 2009, Larry Bock, a venture capitalist, in collaboration with a number of companies, institutions and associations organized the San Diego Science Festival, an effort to educate K-12 students about science through many events.

In addition to these initiatives, the local community initiated a number of collaborative efforts to tackle community issues. In 2005, they formed the San Diego CIRM Readiness Coalition to locate the California Institute for Regenerative Medicine; they formed a collaborative platform, the CleanTECH San Diego, to boost energy and environment-related industries; CONNECT and BIOCOM embarked on several programs to help entrepreneurs access early-stage funding; research institutions in partnership with trade associations and individual companies formed research consortiums like the Sanford Consortium for Regenerative Medicine, the San Diego Center for Algae Biotechnology and the West Wireless Health Institute. When SDEDC embarked on a campaign, San Diego: Technology's Perfect Climate, which laid the foundation for the workforce initiatives, Julie Wright (1999), its president and CEO, wrote:

> It is time, however, to learn from our experiments in working together as a region rather than as individual companies, organizations and municipalities and build on them… We believe that solutions to these challenges will require a different kind of thinking – thinking that's creative, inclusive, and collaborative. This vision is premised upon the belief that the most innovative ideas come from bringing together diverse constituencies who often initially believe that they have little in common.

What has happened after a decade of experience and engagement is demonstrated in an account by Joseph Panetta:

> In a broad scale, we work together as a region. So, if the region needs something, we all get together to support it. If we need water, road, electrical power or a new building, you get the support from the whole community – biotechnology, telecommunications, the building industry. We all work together for common cause. (interview)

Overall, the collaborative efforts have helped the biotechnology industry overcome adversities by generating relationships and resources. The robustness of collaborations in

San Diego is, in part, due its organizational platform. The trade associations, including CONNECT, BIOCOM and SDEDC, and UCSD have been the focal point of communication and the base of implementations. One of the reasons for facilitated communication was that each organization's board of directors is comprised of representatives of other community groups. As Jason Anderson (interview), vice president of SDEDC, said, "there is constant communication between" associations, institutions and leaders as they sit on boards of counterparts. The geographical proximity has also heightened the frequency and fluency of communication. Furthermore, the culture of collaboration was shaped by the collective experience of community engagements. At a community level, individuals have learned how to align themselves with partners and have weaved a web of shared meanings and understanding through participating in and interacting at initiatives. The success in sharing understanding with local governments during the early 1990s was important experience for biotechnology entrepreneurs. At that point, most of them had arrived from outside San Diego, so they were not tightly knitted to the downtown business groups and the local government. This experience led to more extensive collaborations with multiple sectors including high-technology industries, research institutions and local governments.

I asked earlier ‘where have the biotechnology companies in San Diego come from?’, and ‘how has the entrepreneurial system been produced?’ This section intended to answer these two questions by piecing together four sub sections: how four groups of entrepreneurs developed practices and applied them in founding biotechnology companies; how individuals have learned to be start-up entrepreneurs or venture capitalists through doing and learning in communities; how angel investments and other specialized practices have developed; how the biotechnology community in association with other technology-based industries has created a culture of collaboration. The essence of entrepreneurial activity in the biotechnology industry is learning and practicing the process of biotechnology business from identifying commercial possibilities from science, composing storylines, communicating with multiple stakeholders and orchestrating collective efforts to attracting financial resources. It is always people who create, interpret and translate knowledge and practices, but it is their communities where the learning process takes place. Situated with issues and problems and surrounded by companions, individuals are required to tackle issues constantly and continuously by collaborating with colleagues. In the process, they develop skills and understanding on-the-job, and share them with co-workers. The collaborations and conversations with partners not only promote learning process, but also give comfort and confidence. In this sense, the root of start-up activity in San Diego is the actions and interactions in communities, which, as a result, have produced a class of entrepreneurs and experts. Each of them has engaged in creating a series of biotechnology companies and the institutions in San Diego. The culture of the San Diego community is the product of continuous interactions and engagements, at least, over the last two decades. It was not implanted, planned or enforced, but it was constituted as individuals and organizations have shared understanding through daily interactions. Certainly, the presence and prominence of research institutions have been critical to bringing in and training scientific talent, and produced scientific breakthroughs, around which groups of entrepreneurs have created companies and communities. A number of scientists from research institutions have become core constituents of each community: some participated as scientific founders or advisers while remaining in academia; some left universities to become serial entrepreneurs.

# CHAPTER 6: DEVELOPING RELATIONSHIPS

To understand the genesis and growth of biotechnology industry in San Diego, we need to shed light on the impact and involvement of local academic institutions. As discussed in the literature review chapter, the impact and role of universities are different between regions and industries. There is a significant variance between academics in their engagement with industries. I begin this chapter by looking at the differences between academic research and commercializing activity. I argue that the two sectors – academia and industries – are built on distinct skills, resources and rules, thus the differences hinder the translation of basic scientific understanding into medical treatments. Therefore, to translate academic discoveries into products, universities and academic scientists need to develop understanding and practices that help bridge the gaps. In the next sections, I present the science policy of the federal government, which has shaped the research university system, and the institutional efforts of UCSD and non-profit research institutions to manage their relationships with industries. Then, I describe how five academic scientists have developed their understanding, practices and relationships, which are necessary for collaborating with industries. In the last part, I discuss how academics learn to be comfortable and capable of translating basic research into products through hands-on experiences and engagements in communities. Their learning experiences involve participation in entrepreneurial activity, interactions with entrepreneurs, communication with cohorts and conversations at networking events. I conclude that the patterns of academia-industry interactions in San Diego were constructed by frequent and collegial interactions in communities.

## 6-1. Barriers to Knowledge Transfer

UCSD and research institutions in La Jolla and their scientists have been crucial to building the San Diego biotechnology cluster along with their neighbors in the industry side. Talent and research knowledge from academia have fueled the development of local industries, as exemplified by Irwin Jacobs, founder of Linkabit and Qualcomm, and Ivor Royston, founder of Hybritech. Although San Diego is now regarded as one of a few places "where scientists can be entrepreneurs" (Philip Low, interview) and interactions between research institutions and industry are robust, such intimate relationships did not exist from the start. At the same time that a set of practices and resources emerged through learning and interacting process among entrepreneurs, the research institutions, including UCSD and their scientists in La Jolla, have learned and developed programs and practices necessary to commercialize basic discoveries.

In essence, academic research is not turned into applications by itself. Technology transfer requires personal involvement of academic scientists because a large portion of knowledge embedded in discoveries is tacit and embodied. Furthermore, while knowledge and resources for development efforts, including applying, manufacturing and marketing, exist in the realm of industry, most basic research is done in academic settings. The two sectors – academia and industry – exist based on distinct sets of practice and norms. The ways of dealing with problems and necessary skill sets, norms, goals and disciplines are different between the two communities. Academic scientists focus on understanding biological mechanisms and processes related to living organisms. Academics spend most of their time in experimenting and writing with their graduate students and post-doctoral fellows in their laboratory. A large portion of funding comes from federal agencies, including the NIH, which distribute their extra-mural grants based on scientific merit through the peer review process. Academics participate in their scientific community by publishing papers; they secure positions at universities and funding from government agencies. To most academics operating a laboratory and keeping pace with evolving scientific knowledge requires full commitment. In this sense, many academic researchers are too busy to engage in activity outside their university positions.

The ultimate objective of academic research is to contribute to expanding scientific knowledge through publication and education. Academic scientists are mostly interested in understanding the complexity of the natural world without much attention to applications because to academic scientists "the asset that is most valuable is the publication and reputation" (Mark Crowell, interview). Graduate students and post-doctoral fellows look at a track of publications and awards of faculty when they choose their training destination. The discrepancy between research and practical applications is wider for academic researchers whose research is concerned with meta-theories or pure science. They normally have neither an interest in nor relevance to commercialization of their research. Researchers in pure science have few interactions with and interest from industry, thus rarely they become involved in entrepreneurial activity to develop applications.

Most faculty members at universities run their laboratory as an independent entity that consists of a group of post doctoral fellows and graduate students. They compete for grants and publications with their colleagues working in the same field. In most times, they run their laboratory and research projects as an independent agent by deciding directions and approaches on their own. To run a business, people at a company have to operate as a team by sharing information, consulting with colleagues and aligning themselves with the entire organization.

To scientists in industry or entrepreneurs, developing products and earning profits are their main concern. While academic culture gives more emphasis on openness, sharing and publication of research, as Mark Crowell (interview), who has been involved in transferring technology at universities for decades, noted," on the corporate side, it is secrecy, the return of investment and profitability." The funding for commercial development comes from the private sector including venture capitalists, institutional investors, corporate partners and a public market. The core mechanism of allocating financial resource, so-called 'due-diligence,’ that focuses on potential returns from investments.

Differences associated with a lack of mutual understanding often lead to a misconception or even antagonism between academia and industry. The lack of understanding or experience deters flow of knowledge in two ways: academic scientists having no experience with industry tend to regard running or participating in companies as the same as doing scientific research in their laboratory. Therefore, they apply the know-how, skills and practices that they developed and acquired by doing basic research to founding and running companies. Michael Krupp, an adviser at the von Liebig Center, pointed out this misunderstanding of academics:

> They [academics] think running a business is easy. They think it does not require any particular skill nor realize there are a variety of things. To be worse, some people coming out of academia do not know when to engage outside experts and managers. They want to do everything themselves. (interview)

As a second issue, the lack of understanding sometimes leads to hostility toward industry. Some academics intentionally avoid interactions or communication with scientists in industry believing industrial science is inferior and impure. In some cases, faculty feel uncomfortable in collaborating with industry finding themselves at odds with practices and culture of industry. Gary Firestein (interview), dean of the Translational Medicine at UCSD, observed that in this way: "There are some people in the university setting that view science in industry as being somewhat lower quality compared to individuals who are in the ivory tower of academia."

Although academic research has been instrumental in nurturing and nourishing the biotechnology industry, the development of therapeutics should involve a set of skills, practices and facilities outside of universities. Howard Greene, former CEO of Hybritech, explained the gap between basic research and development efforts: "There is a major difference between a scientific breakthrough and a product. There's a great deal of distance between the laboratory and the hospital" (Berger 1984c). Translation of academic research into treatments requires a stream of diverse expertise, skills and resources as told in the first section of Chapter 5. (Also, Table 6-1 gives a brief summary of the drug development process.) Besides clinical trials, modern-day drug research and discovery involves multiple disciplines and techniques: "molecular biology, cell biology, genetics, bioinformatics, computational chemistry, protein chemistry, combinatorial chemistry, genetic engineering, high throughput screening, and many other fields" (Pisano, 2006, p. 11). Therefore, an academic scientist specialized and experienced in one discipline has only limited capacity in the drug research and development process.

Moreover, the functions and facilities for clinical trials and regulatory procedures lie outside the boundary of academic setting. But to develop drugs, a large part of resources and expertise must be devoted to conducting human clinical trials and communicating with the FDA. Troy Wilson (interview), a founder of several biotechnology start-ups, described the distinctive capabilities: "Universities are very good at making basic science and making basic discoveries. In general, universities do not do good job at doing development, whether it is product development or clinical development. That's just not what they're good at." Academic researchers employ 'scientific methods' to explore or explain their research inquiries. Many of these inquiries have not ever gone into experiments before. In contrast, according to Wilson, the development process is more like "doing things that have been done hundred times, thousand times before." The expertise on the development process is experience and understanding on "what the Food and Drug Administration (FDA) is looking for, and who can help you work that compound through the process preparing it for an FDA review."

**Table 6-1.** Drug discovery and development process

| Process | Goal | How | Compounds (Years) |
|---|---|---|---|
| Pre-discovery | Understand the disease and choose a target molecule | Scientists in pharmaceutical research companies, government, academic and for-profit research institutions contribute to basic research | |
| Discovery | Find a drug candidate | Create a new molecule or select an existing molecule as the starting point. Perform tests on that molecule and then optimize (change its structure) it to make it work better | 5,000 - 10,000 (3-6) |
| Preclinical | Obtain FDA approval to test the drug in humans | FDA reviews all preclinical testing and plans for clinical testing to determine if the drug is safe enough to move to human trials | 250 |
| Phase I Clinical Trial | Discover if the drug is safe in humans and estimate safe dosing range | Test with about 20 to 100 healthy volunteers | 5 (6-7) |
| Phase II Clinical Trial | Evaluate the drug's effectiveness and examine any side effects and risks | Test with about 100 to 500 patients with the disease or condition under study | |
| Phase III Clinical Trial | Generate statistically significant data about safety, efficacy and the overall benefit-risk relationship of the drug | Test with 1,000 to 5,000 of patients | |
| New Drug Application and FDA Review | FDA reviews results of all testing to determine if the drug can be approved | The FDA reviews hundreds of thousands of pages of information, including all clinical and preclinical findings, proposed labeling and manufacturing plans. They may solicit the opinion of an independent advisory committee | 1 FDA-Approved Drug (0.5-2) |
| **Total** | | $800 million – $1 billion | 1 out of 5,000 to 10,000 (10-15) |

*Source:* Pharmaceutical Research and Manufacturers of America (PhRMA), 2007.

Academia is often not equipped with facilities or expertise required to develop basic research discoveries into products or processes. At universities, according to Dennis Carson (interview), director of UCSD Cancer Center, "there is not good infrastructure for translational work like manufacturing, toxicity, regulatory. We don't have that infrastructure." This barrier is particularly challenging to academic researchers and universities if they seek to develop applications on their own. Academic researchers might benefit from learning expertise necessary to run a company and developing relationships with industry from the ground up. Universities or research institutions confront the same obstacle when they want to develop basic research into applications in-house.

On the business side, academic people's lack of understanding on the entire process of drug development and difficulties involved in the biotechnology business constrains collaborations and communication between the two sides. Kleanthis Xanthopoulos, a founder of a series of biotechnology companies, described the communication gap that comes from the lack of understanding:

> It [academic research] is a step of 100 step-ladders if you are invested in developing ultimately a drug. Your idea has to go through so many steps. I think that is the disconnect. Because people at academia don't know that process well, they have tendency to underestimate the value of that process. (interview)

To many entrepreneurs, staff of technology transfer at universities and academic scientists demand too many benefits without sharing the risks and burdens of developing basic research commercially.

Furthermore, the two communities operate on distinct timelines. Academic scientists are "basically independent contractors who work on what they want to do" (Abgail Barrow, interview), but entrepreneurs must coordinate schedules with many partners and co-workers. What is most crucial to academic people is to publish their discovery than do complete projects within a given timetable. Jane Moores (interview), director of the Technology Transfer Office at UCSD, described it this way: "Academia is less focused on finishing a particular task by a particular time, they give more focus on the curiosity-driven nature of research. To industry, timeline is very critical and important."

The two groups –academia and industry – employ distinct practices in doing research. Jonathan Chesnut (interview), director of stem cell research at Life Sciences, described how scientists in industry pay attention to "how they can manufacture cost-effectively as well as whether market exists," while academic scientists are mostly interested in the possibility of publication. He continued to point out that the practice of dealing with intellectual property is different: working on what academic researchers did, industrial scientists have to "look to see what intellectual property there is" because academic researchers do not pay enough attention to it.

Another significant barrier to turning academic research into applications lies in regulations and restrictions imposed by universities and federal agencies. Technology transfer, as noted in a report prepared by a group of scientists at UCSD (University of California, San Diego, 1987, p. 7), is "essentially a people business. It is the individual who revolutionizes the scientific world with his or her cutting-edge concepts." In most cases, academic scientists participate in development efforts either as scientific founders, consultants or scientific advisers even though their inventions are patented and licensed to a company. In the process, issues of conflict-of-interest and conflict-of-commitment arise. As members of universities, they are required to disclose any patentable inventions, report financial interest arising from their engagements with companies, any professional activities outside of university and any kinds of sponsorship from industry to their laboratory.

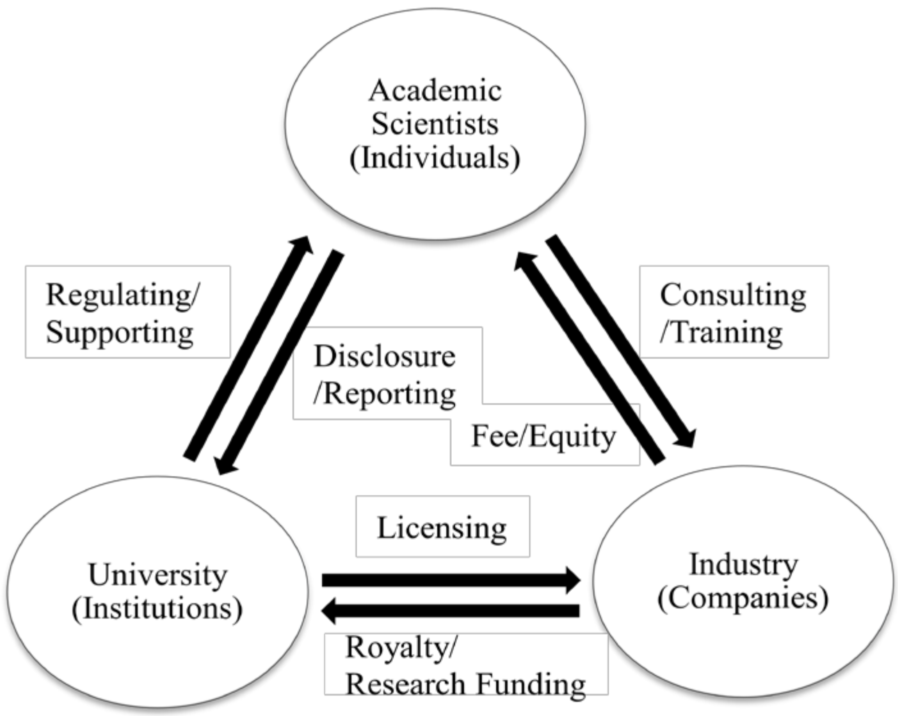
This requirement is particularly burdensome when full-time faculty members seek to establish and manage a company rather than be involved as an adviser or consultant. These scientific founders, who have their appointment at universities, own a majority of ownership and make decisions of their company, which can result in conflict-of-interest. Under this condition, these scientific founders may make decisions in favor of their companies. They may spend research funding to help their companies rather than to abide by academic norms. Start-up and management activity, in most cases, require a full commitment, which may lead to conflict-of-commitment. Due to the regulatory scheme, faculty have to leave or take absence from academia to fully commit to entrepreneurial activity. Thus, the regulations limit involvement of academic researchers with industry to a minority role or stake. Along with regulatory schemes, penalties and blame on faculty members who violate the rules and guidelines, either by not disclosing their engagements in industry or exploiting the relations with industry illegally, discourage newcomers from embarking on any entrepreneurial initiatives.

In addition to the existence of regulations, ambiguity in regulations and costs involved in complying with rules makes academics who intend to interact with industry feel uneasy and uncomfortable. The report, the Biotechnology Transfer Process, (University of California, San Diego, 1987, p. 21) notes that that "several faculty indicated a faculty advisory committee should be formed to provide information to faculty who are unaware of industry support." To this end, the report suggested that the university establish a Technology Transfer Advisory Committee on the campus to develop standardized guidelines and to guide faculty through their interactions with industry. The report drew attention to the necessity of introducing more explicit and comprehensive guidelines with the following recommendation:

> One of the most important suggestions arising from the study committees' discussions is the desire to develop standards wherever possible... One of the University's difficulties in providing consistent treatment based on the systems and safeguards already inherent in the current system is due to the fact that many situations are handled on a "case-by-case" basis. There are circumstances that may be unique to any case, however, it is believed with the experience of UCSD and other institutions in the transfer area it is indeed possible and desirable to establish standardized expectations, clauses, licenses, and scenarios for university/industrial relationships. (p. 71)

By the same token, companies must abide by regulations and policies set by universities when they seek to commercialize academic inventions either by licensing them from university's technology transfer office or doing cooperative research with academic laboratories. To license any patented or patentable technologies, terms and conditions for contracts must be in accordance with university policies. This is also the case when a company employs academic scientists as consultants or appoints them as scientific advisers. The relations should be consistent with regulations on conflict-of-interest and conflict-of-commitment. The relations between three agents – academic scientists, industry and universities – in Figure 6-1 indicate that the institutional arrangements at universities can be a substantial obstacle to academia-industry interactions.

**Figure 6-1.** Three-way relations between individual scientists, industry and university




Obstacles arise from lack of understanding and misperception. In negotiating with the conditions and terms of licensing agreements, each side is often at odds with practice and culture of the other side. An entrepreneur, Kleanthis Xanthopoulos (interview), described the difficulty in interacting with technology transfer offices: "Not only are we in different ballparks, but we play different games: we play soccer, and they play American football." To the industry side, the staff at the technology transfer office have tendency to underestimate the cost and risk involved in commercialization because, Xanthopoulos continued, "they at academia don't know that process." Similarly, Troy Wilson, a founding CEO of biotechnology start-ups, observed that: "they don't have a good sense of how much work it is to actually go from a basic research invention to a product. They don't understand how much time is involved, how much money is involved, how much risk is involved. They think, in some cases, small companies or large companies try to cheat them out of their fair share." In this regard, to be more productive, the technology transfer office should, according to Wilson, "know what the game is, and they should figure out 'what is the winning technology.'" For example, a report by UCSD (1987, p. 21-22) criticized the practice of their licensing office: "the University licensing department has a tendency to approach licensing from a legalistic point-of-view, rather than a business perspective." To be successful, the report recommended that the department "approach technology transfer from a business win/win perspective." When the technology transfer office develops a set of standardized terms and practices, the people on the industry side can become more comfortable.

Countering the argument, Alan Paau (2004), former director of UCSD Technology Transfer Office, ascribed the complaints from industry to their lack of understanding of the institutional context of universities:

> The academic technology transfer process at times is viewed by industry as cumbersome because there is a genuine cultural divide. Industry is, rightly, profit driven. Academia is more "public good" driven. We include in our licenses terms that protect taxpayers, small businesses, our tax-exempt status, our academic missions, our nonprofit charter and the public.

A remark by Mark Crowell (interview) supports Paau's point of view: "the difference between academic culture and corporate culture" is what hinders collaborations.

**Table 6-2.** Differences between academic research and commercializing activity

| | **Basic Research** | **Applied Research** | **Development** |
|---|---|---|---|
| Stage | Research<br>(Pre-discovery) | Discovery<br>(Translational Research) | Development<br>(Preclinical Trials/ Clinical Trials) |
| Players | Universities<br>Non-profit Research Institutions<br>(Pharmaceutical & Biotechnology Companies) | | Pharmaceutical and Biotechnology Companies |
| Funding Sources | N.I.H/Federal Agencies<br>Foundations | SBIR/STTR<br>Angels/Foundations | Investors: Venture Capital, Private Equity Fund, Corporations, Public |
| Funding Mechanism | Peer Review | | Due-Diligence |
| Main Goal | Advance Scientific Knowledge | Ascertain Applicability of Scientific Discovery (Proof-of-Concept) | Apply Sciences in Developing Solutions |
| Objectives | Identify Targets & Mechanisms | Create Drug Candidates & Test Applicability | Prove Safety & Efficacy in Humans |
| Culture | Openness<br>Independence | | Exclusiveness<br>Coordination |
| Motivation | Reputation & Respect from Peer Groups<br>(Publish or Perish) | | Profit & Profile at Marketplace<br>(Proceed & Produce) |
| Rules & Codes | Conflict-of-Interest<br>Conflict-of-Commitment | | |
| Setting | In-vitro Experiments<br>(Laboratory) | In-vivo Experiments<br>(Laboratory/Hospitals) | Human Clinical Tests<br>(Corporation/Hospitals) |
| Partners (Evaluators) | Peer Group<br>Review Panel | | Hospitals/ F.D.A<br>Investors/Customers<br>Shareholders |

Overall, the practices and norms of academic research have evolved in a way that "scientists may work in an atmosphere which is relatively free from the adverse pressure of convention, prejudice, or commercial necessity" (Bush, 1999[1945], p. 19). The two sectors have developed practices and norms to achieve distinct goals in different organizational settings. Regulations and guidelines have been instituted to guard freedom and openness of academia from any commercial interest and interventions, but at the same time to allow academics to pursue entrepreneurial endeavors to a certain degree. Basic research conducted at an academic setting by academics must move along the process of drug development that has been practiced by biotechnology and pharmaceutical industries. Table 6-2 specifies the different rules and resources between academics and commercial developers. Any academic scientists having long-term training and experiences at academic laboratories would likely be unfamiliar with development efforts of industries. This is also the case with industrial people, who do not have exposure to academia: they would likely to have difficulties in interacting with academic scientists. Therefore, the most important hindrance to technology transfer is the gaps in practices, norms, regulations and resources between academia and industry.

## 6-2. Institutions Governing Industry-University Relations

The University of California was founded in 1866 based on funding from the 1862 Morrill Land Grant Act. The university was originally named 'the Agricultural, Mining and Mechanical Arts College of California', indicating its origin from the land grant. In 1868, the University of California was chartered in the state constitution. On the one hand, the university was founded to serve society, but on the other hand, the university was enacted to be an independent institution for education and research. A report notes the tension between these two missions: "the University has a social responsibility to sustain the diversity of its research activities and to continue its tradition of independence from undue influence by a single source" (University of California, 1982, p. 5).

Relations with industry did not draw much attention from the public and the university until the late 1970s. Debates and institutional efforts related to governing relations with industry surfaced as a main issue from the late 1970s and the early 1980s. First-tier universities like the University of California had devoted their attention and resources to be 'research universities' by securing contracts and grants of the federal government. After World War II, the federal agencies instituted a variety of granting and contracting programs to achieve their organizational objectives by supporting and leveraging universities and research institutions (Blanpied, 1998). The blueprint that shaped a framework for science policy after World War II was Vannevar Bush's (1999[1945]) report, S*cience -The Endless Frontier*, which was reported to President Truman. In the report, Bush argued that the federal government should be the primary funding source for basic research and training at universities and research institutions to maintain its leadership in medicine, military and economy.

Bush (1999[1945], p. 10) claimed that industrial innovations would flourish based on advances in basic science: "new manufacturing industries can be started and many older industries greatly strengthened and expanded if we continue to study nature's laws and apply new knowledge to practice purposes." And most basic research and training that produces and disseminates “general knowledge and an understanding of nature and its laws” (p. 18) must be conducted at universities, colleges and research institutes, not by government agencies or industry. Bush argued that freedom of inquiry is the most crucial condition for basic research, and it is in these independent academic institutions: "scientists may work in an atmosphere which is relatively free from the adverse pressure of convention, prejudice or commercial necessity" (p. 19). Influenced by Bush's report and political decisions, the federal government and the academic community instituted science policy and practices that placed the federal government as the primary sponsor of basic research and focused on upholding “the free play of free intellects” (Bush, 1999[1945], p. 12).

Federal agencies, including the National Science Foundation (NSF) and the NIH adopted the 'peer review process' as a basic mechanism to disburse their grants and contracts. It is scientific merit evaluated by a peer group of scientists that determines a selection of proposals, not implications or impacts for industries. Moreover, the yearly expansion of the federal R&D funding after World War II was plentiful to academics and universities, so they were not interested in seeking support from industry, as Atkinson (interview) stated: "years after World War II, there was so much federal money flowing to universities from, for example, NASA and the Department of Defense. So, universities no longer sought cooperation with industries and became almost an island." In virtue of the science policy and federal funding after World War II, American universities have become the powerhouse of scientific research and training in the world, but the strength of basic research did not lead to the prosperity of American economy.

From the 1970s, the U.S. began to feel its vulnerability to the emerging economies, particularly Japan. Its manufacturing base was being encroached by Japanese conglomerates, and the eclipse of manufacturing industry raised a national concern. Amid debates on national competitiveness, the insulation of academia from industry began to be viewed as an importance factor in the declining manufacturing (Mowery, Nelson, Sampat & Ziedonis, 2004, Ch. 5). One of the initiatives to address the concern was to allow universities to hold title to their inventions and to license them, even exclusively, to industry by enacting the Bayl-Dole Act of 1980. Prior to the enactment of the Bayh-Dole Act, federal agencies retained title to inventions developed under federal funding, and federal agencies had the right to patent and license the inventions (Council on Governmental Relations, 1999; Bremer, 1998). Under this system, universities were much less motivated to patent and license research discoveries, and industries were reluctant to investing in academic inventions because the federal agencies licensed inventions non-exclusively. Furthermore, universities needed to deal with separate patenting and licensing policies of 26 federal agencies, which provide funding for academic research because a uniform patent policy did not exist (Bremer, 1998).

Another important policy initiative to tackle the competitiveness crisis of the 1970s and early 1980s was the creation of the Small Business Innovation Research (SBIR) program in 1982 (Audretsch, 2001a). This program was to unleash the creative power of small companies or entrepreneurs by providing them early exploratory and technology developing funding. The SBIR program mandates major federal R&D departments and agencies to disperse 2.5 percent of their R&D funding appropriations to small businesses.

Funding is awarded through the peer review process, which focuses on scientific and technological merit. Similarly, the Small Business Technology Transfer (STTR) program was introduced to facilitate partnerships between small businesses and universities in commercializing academic research. The program requires five federal agencies to spend 0.3 percent of their R&D budgets in supporting collaborative R&D efforts between small firms and research institutions. In the fiscal year of 2009, the NIH awarded $577 million and $74 million through the SBIR program and the STTR program, respectively. These programs have encouraged and enabled academic scientists to pursue entrepreneurial activity through creating start-ups.

The evolution of these institutions and programs has given incentives to universities and academics to embark on institutions and endeavors for promoting commercialization of basic research. At the same time, the emergence of biotechnology and its involvements with academics unleashed another wave of opportunities and interests in technology transfer activity among academic scientists (Kenney, 1986). A series of early biotechnology companies has emerged from partnerships between academic researchers and venture investors – most notably, Genentech by Herbert Boyer, a professor of UCSF and Chiron by William Rutter, a chair of Department of Biochemistry and Biophysics at UCSF (Chandler, 2005) in 1976. From the beginning, the University of California was one of the academic centers which fueled the development of biotechnology industry. According to a 2003 report (Yarkin & Murray, 2003), one out of three biotechnology firms in California was founded by scientists from the University of California.

Universities needed to regulate their academics' interactions with industry, but also they recognized the opportunity for increasing research funding. Research contracts with biotechnology and pharmaceutical companies emerged as an important source of funding to universities (Kenney, 1986). Also, income from licensing academic inventions started draw attention as another alternative funding source besides federal funding and state appropriations. Amid the increasing attention to and interactions with industry, in 1999 the university sued Genentech alleging the company had misappropriated the university's patented gene to develop a growth hormone therapy. In 1999, Genentech offered $200 million to the university to settle the legal dispute (Abate, 1999; Ristine, 1999). As the engagements with industry increased, these activities drew more concerns and criticisms from insiders and outsiders. The university has been lauded as the engine of California's innovative economy, but at the same time, the university had to develop and enforce regulations on the relations with industry.

Regulations and policies regarding interactions with industry have revolved around three issues: intellectual property rights; conflict-of-commitment; and conflict-of-interest. In 1982, the University of California instituted a comprehensive guide to regulating various modes of relations – the Interim Guidelines on University-Industry Relations (University of California, 1982). The purpose of the guide was to ensure that the interactions happen without deteriorating the principles as a public research institution. The guidelines stated that any cooperative efforts should not disrupt openness and freedom to publish. However, the guidelines allow a delay of publication for a limited period by stating "no more than sixty days is reasonable" (p. 9). Related to consulting activities of faculty, it mandated faculty who were involved with companies to submit an annual report on such activities. In 1989, 'the Guidelines on University-Industry Relations' replaced the preliminary policy, and it gives more specified and formalized references. The new guidelines issue five principles: “open academic environment”, “freedom to publish”, “the obligation to avoid conflict of interest”, “disclosure responsibilities” and “responsibility to students.”

In terms of patenting, the university adopted a formal policy in 1943, but it was 1963 when every employee was mandated to disclose inventions and assign patents to the university (Matkin, 1990). With the policy of 1963, the university increased the inventor's share of royalties to 50 percent from the previous range of 25 to 15 percent to promote invention disclosures – in 1997, the university reformulated the distribution of royalty income by allotting 15 percent of it to an inventor's campus or laboratory, while dropping the portion of inventor(s) to 35 percent. Until the late 1980s, a system-wide centralized office managed patenting and licensing. This centralized system, as opposed to a campus-based practice, was often pointed out as a barrier to improving industry relations and developing practices (University of California, 1982; University of California, San Diego, 1987).

In 1986, the Council of Chancellors made recommendations regarding the patenting system: the assignment of royalty income to each campus or laboratory, and the establishment of in-house campus program or organization to support patenting and licensing nearby (University of California, San Diego, 1987). The first campus-based technology transfer office was set up in 1994 at UCSD, the Office of Technology Transfer and Intellectual Property Services (Technology Transfer Office). The implications of a campus-based office were pointed out by Richard Attiyeh, then vice chancellor for research: "most inventions require follow-up work to become commercialized. The expert knowledge of the inventor is essential. Having an office on campus puts companies in closer contact with inventors" (Vezina, 1994).

Another significant regulation of the engagement with the private sector is that employees of UCSD are required to avoid (or manage) any conflict-of-interest. The Political Reform Act of 1974 mandates elected officials to disclose any financial interests possibly arising from their public position. In 1982, California's Fair Political Practices Commission extended the application of the regulations to the employees of University of California. Therefore, the employees of the university have been mandated to disclose any financial interest of gifts, grants or contracts from the private sector. Its objective is to prevent any employees from influencing a decision in favor of one's own financial or other personal advantages. If any potential of financial interest arises, the Independent Review Committee on Conflict of Interest intervenes. The regulations were adopted by UCSD in 1982, and a formalized document – the Policy and Procedures Manual (PPM) 200-13 – was issued in 1984.

Regarding conflict-of-commitment, the University of California instituted a guiding policy on outside activity of its employees in 1958, titled Regulation No. 4. The faculty members of the University of California have responsibilities of fully committing themselves to the university's mission: teaching, research and public service. Under this regulation, employees were allowed to engage in outside activities only if these activities do not interrupt their commitment to the university, and they are related to their duties of teaching, research and public service.

For individual faculty, the personal involvement in outside activity has been regulated by a set of codes and guidelines. If any active faculty members want to engage in outside activities, such as managing and consulting companies, they should abide by the conflict of commitment rule. In 2001, the University of California revised the Conflict of Commitment and Outside Activities of Faculty Members (APM - 25). Prior to the revision, outside activities of the faculty members had been governed by the one-day-per-week rule (Drummond, 2003). Faculty was allowed to conduct activities outside the university duties for one day per a week.

The 2001 revision created "mechanisms to ensure that activities outside the University do not interfere with fulfillment of these responsibilities" (University of California, 2001). The rule pinned down allowable days spent on compensated outside activities–one day per week which is 39 days a year for a full-time faculty member on an academic-year appointment–and imposed responsibility of annual reporting on such activities. Under this rule, for example, holding an executive or managerial position is principally forbidden. Providing consulting services to or serving on the board of directors of private businesses are allowed within the 39 day time limit without any prior approval.

In contrast to the efforts to institute regulatory frameworks which constrain or manage industry-related activity, the university embarked on initiatives to facilitate interactions with industry. In 1996, the Industry-University Cooperative Research Program (IUCRP) was launched to promote interactions between academics and industry. Through the program, research grants, named the UC Discovery Grants, are given to its faculty and researchers having matching fund from industry. The grants were introduced, not only to provide seed funding, but also to encourage involvement with industry partners. To participating companies, the matching fund "enables them to leverage their slim assets by sharing the university's experience, equipment and expertise" (Penhoet & Atkinson, 1996). The program, as Edward Penhoet, president and CEO of Chiron Corp, and Richard Atkinson (1996), president of the University of California, pointed out, is intended to facilitate technology transfer through "one-on-one involvement."

The federal government has adopted policies such as the Bayl-Dole Act of 1980 and the SBIR program to promote technology transfer. At the same time, the University of California has enacted rules and specified guidelines to provide a more standardized reference to its employees so they can interact with industry within boundaries. The evolution of regulations, in large part, reflects the increasing demand for participation of academics in developing practical applications while maintaining freedom and openness of scientific inquiry. Along the way, UCSD has constituted its own institutions and programs to regulate and also encourage technology transfer activity.

## 6-3. Historical Evolution of Industry-University Relations of UCSD

From the beginning, founding faculty of UCSD focused on building a first-class research university by recruiting renowned scientists who would eventually bring funding and graduate students. The vision was to create a sanctuary for scientific research. Faculty at UCSD identified their locality as La Jolla rather than San Diego, which was one of their ways to detach from San Diego. Most of all, until the early 1980s, the university, as Daniel Pegg (interview) noted, "was focused on building itself and had been an entity onto itself." William Fenical (interview), a long-time faculty member of UCSD, described the relationship with industry in this way: "about twenty five years ago, the university was considered as ivory tower. If you were working with industry, you would be considered a black mark. You sold out the ivory tower."

Partnerships with the local community were not seriously conceived or sought by the founders of UCSD. Furthermore, as a campus of the University of California, activities and endeavors of UCSD were restrained by the policies and regulations of the UC system. In 1964, the campus enrolled undergraduates for the first time, when the Free Speech Movement at the Berkeley campus was gaining national-wide attention. The demonstrations and protests to the escalation of Vietnam War by the UCSD undergraduates and faculty aggravated relations with politically conservative San Diegans (Shragge, 2001). Until 1980, each campus of the UC system was restricted from raising fund from the private sector. In 1960, Clark Kerr, then president of the University of California, drafted a policy guiding its campuses not to compete with private universities in their efforts to raise funding (Scott-Blair, 1985). The restriction on fund raising from the private sector became invalidated as each campus launched large scale private fund raising campaigns from 1980. No endowed chair existed until 1981 at UCSD. Efforts to raise funding for the UCSD Foundation and for building a performing art center on campus failed to bear any significant fruit until the early 1980s (Anderson, N., 1993).

Beginning 1981, UCSD launched full-fledged efforts to raise private funding and by 1985, the campus installed 19 endowed professorships (Scott-Blair, 1985). In 1985, UCSD succeeded in landing the Supercomputer Center in San Diego – one of five centers in the country funded by the National Science Foundation – by leveraging a partnership with General Atomics (Berger, 1985a). Along with these successes, a series of failures to attract research consortiums during the 1980s (as mentioned in Chapter 4-6) led the local industry and academic leaders to rethink their relations. In 1985, the university launched CONNECT in partnership with the local community. Since then, the university and its schools have accelerated the development and implementation of a set of partnerships to enhance the local knowledge and entrepreneurial base. As shown in Table 6-3, by 1980, about 90 percent of R&D expenditures of UCSD stemmed from the federal and state governments. From 1980, a portion of R&D funding from non-governmental sources started to grow substantially, and it accounted for 38 percent of the entire R&D expenditures in 2008.

**Table 6-3.** Sources for R&D expenditures of UCSD (1972-2008)

($ thousands)

| Year | Federal Govt. | State/Local Govt. | Industry | Institution | Other | Total | % of Non-Govt. Sources to UCSD (Entire Univ. and Colleges) |
|---|---|---|---|---|---|---|---|
| 1972 | 52,295 | 150 | - | 2,943 | 1,919 | 57,307 | 8.5 (21.5) |
| 1975 | 69,032 | 365 | - | 4,268 | 3,233 | 76,898 | 9.8 (23.2) |
| 1980 | 111,038 | 648 | - | 6,176 | 6,968 | 124,830 | 10.5 (24.3) |
| 1985 | 115,632 | 642 | - | 14,092 | 15,184 | 145,550 | 20.1 (29.6) |
| 1990 | 182,555 | 4,922 | 9,135 | 23,145 | 17,275 | 237,032 | 20.9 (32.7) |
| 1995 | 284,445 | 9,208 | 11,363 | 26,623 | 25,694 | 357,333 | 17.8 (32.3) |
| 2000 | 326,037 | 23,691 | 34,541 | 87,632 | 46,658 | 518,559 | 32.6 (34.4) |
| 2005 | 463,946 | 18,051 | 34,259 | 121,741 | 83,038 | 721,035 | 33.2 (29.8) |
| 2008 | 490,963 | 30,649 | 49,878 | 141,291 | 129,246 | 842,027 | 38.1 (33.3) |

*Data Source*: National Science Foundation, WebCASPAR: NSF Survey of R&D Expenditures at Universities and Colleges (1972-2008) Retrieved from http://webcaspar.nsf.gov/index.jsp?subHeader=WebCASPARHome on February 24, 2010

Richard Atkinson, Chancellor of UCSD from 1980 to 1995, came to UCSD in 1980, and was crucial to changing the attitude and attribute of the university to be more interactive with the local community. Atkinson, as Daniel Pegg (interview) claimed, "brought in a broader view of university's role in the community and that was when we began to be more involved." Atkinson's primary objectives were to enlarge and diversify the university's funding base, which was fundamental to enhancing the university's research capacity. Atkinson (interview) explained: "I personally believe that everything depends on whether the university really believes in research and really believes in supporting the faculty members who are capable of making contributions." At the same time, he was committed to enhancing the relevance of academic research to the social and economic activity by facilitating applications. Atkinson emphasized the importance of enabling faculty to pursue commercial applications of their research:

> If a faculty member involved in research says 'we reached the point where you can see the potential for applications', the university has to create an environment in which that person can pursue that. We put huge emphasis on being a very active research university and pushing research that has any applications in the private sector. (interview)

In short, he and the university intended to capitalize on a synergy with the local industry. As Daniel Pegg (interview) recounted: "by teaching and helping people, the university recognized some of the benefit could come from the private sector. To private sector, they understood outstanding resources were available from the university." The local community also began to recognize the mutual benefit of collaborations and has initiated or participated in industry-university collaborations (refer to Chapter 4-6 for the coming of a new perspective).

One of Atkinson's initiatives was to design and offer training programs to scientists and engineers at the local high-technology companies through its division of extension. Mary Walshok was appointed as Dean of the UCSD Extension in 1981 by Atkinson to lead the initiative. The UCSD Extension launched a new program in 1984 – the Executive Program for Scientists and Engineers – to help local scientists spearhead their business ability. Walshok (interview) said of the significance of the new program: "There was no local management education or executive education for people working in R&D institution and in science-based companies. We were teaching real estate [agents], corporate lawyers and small family businesses." The traditional programs were neither tailored for high-technology businesses nor appropriate to scientists.

CONNECT was another early campus-wide initiative to bring the university close to industry. People on the industry side began to visit the UCSD campus to participate in the programs of CONNECT. CONNECT ran a series of seminars where academic and industrial scientists presented their discoveries to public. For example, academic scientists who wanted to start up a company were provided coaching and networking opportunities by participating in the Springboard program. Abigail Barrow, a director of the Springboard program, described the impact of the program:

> We got hundreds of people from the community into those events. That opened up what academics were doing, what were happening in the business community. It also soon networked more people from the research side with people from the business side. It was opening the door. (interview)

Various activities organized by CONNECT helped open the gate of the university to the local community, and it also contributed to exposing faculty to the local entrepreneurs. Involvement and contacts through programs like CONNECT helped people from one side know, understand and trust people from the other side. About the formation of personal trust and relationships, Walshok explained:

> Scientists know attorneys, accountants and many marketing people. People in the industry side also know chemists and biologists before they ever work together officially to grow a company. I think this is the secret of CONNECT. (interview)

The familiarity, trust and shared knowledge have been pivotal in starting university-industry partnership initiatives as well as proliferating technology-based start-ups.

In 1986, the School of Medicine formed the Biotechnology Transfer Study Committee to survey the issues related to technology transfer and to suggest recommendations. Following one year of surveys and interviews, the school published a report entitled 'A study of the biotechnology transfer process'. In the report, the committee proposed that a campus-located technology transfer office and Technology Transfer Advisory Committee be established (University of California, 1987). The School of Engineering and the School of Medicine have also been active in encouraging and enabling their faculty to pursue commercial development of academic research. The School of Engineering started the Corporate Affiliation Program and the von Liebig Center for Entrepreneurism (von Liebig Center). The School of Medicine began the UCSD TransMed Program and established the Clinical and Translational Research Institute. Even though they were based on distinctive concepts – corporate partnership of the School of Engineering and translational medicine of the School of Medicine – both schools focused on providing resources and knowledge to their faculty to facilitate commercializing activity.

One of the initiatives that emerged to facilitate the industry-academy collaborations was the Corporate Affiliates Program at the School of Engineering in 1995. In 1994, Robert Conn joined the school from the University of California, Los Angeles as a dean. To elevate and expand the school, Conn sought to capitalize on resources from industry by nurturing academia-industry relationship (Siedsma, 1999b). Once he noted: "neither the state nor the federal governments will be providing the kind of resources to universities that they did during the '50s, '60s and '70s." (Bigelow, 1996) To mould a platform on which the school and industry would interact, he formed a committee to set guidelines and programs.

The Corporate Affiliates Program has been a focal point of interactions between the school and industry. The liaison program, Anne O'Donnell, director of the program, once said, "allows businesses to form a partnership with the engineering school" (Sidener, 2004). Through the program, industry partners participate in research projects by providing matching grant. Events like Research Expo, whereby graduate students present their research projects to public, have also channeled academic talent and expertise to the local industry (Anderson, T., 2004).

The School of Engineering, under Conn's leadership, explored establishing an incubating program during the 1990s. The vision was to assist and motivate faculty by providing proof-of-concept grants and business advice, so they would further develop their laboratory research (Allen, 1996; Andrea, 1996). In 1999, the School of Engineering brought in Jack Savidge, a lecturer at UCSD Extension, and Stephen Flaim, a scientist entrepreneur, to develop a program inside the school (Stephen Flaim, interview). At the beginning, they struggled to resolve two issues: securing funding and designing supporting mechanisms. People engaged in the early process continued to converse and discuss structuring a new program while contacting with the William J. von Liebig Foundation. In 2001, Abigail Barrow joined from CONNECT and structured a new program with Jack Savidge.

In 2001, the School of Engineering launched an incubation center, the von Liebig Center, based on a $10 million donation from William J. von Liebig Foundation. The mechanisms to cultivate the entrepreneurism of faculty include seed funding, advisory services and educational programs (Gulbranson & Audretsch, 2008). Barrow, the founding director of the center, explained the underlying mechanism to cultivate faculty's entrepreneurism:

> We wanted to enhance, improve and encourage more commercialization activity, specifically start-up activity. To make faculty interested in taking their invention to the prototype stage, we have to give a little bit of money, so they can hire post-doctoral fellows, graduate students, and pay some for other services. Otherwise, they don't have much patience to do it. Then, they begin to think about the commercialization process: to take research into industry or investor, what results they need to produce, how they make technologies better and cheaper than existing ones out there. (interview)

Originally, the center granted funding to faculty in the School of Engineering, but beginning in 2008, the center began serving the entire campus – up to $75,000 depending on progress. Proposals are evaluated based on potential and possibility of commercial development by people in business. Barrow (interview) explained the review process: "all reviews were done by people in business, so we weren't doing science review, but we were doing business review and commercialization review." Each grantee is assigned an adviser with extensive experience in industry. Advisers help faculty go through process of business development and connect with potential investors. Along with the funding and mentoring services, the center offers courses on entrepreneurism to graduate students.

Through the funding process, faculty have been assisted and encouraged to become involved in entrepreneurial activity and with people from the industry side. According to a newspaper article, by 2006 more than half of the faculty at the School of Engineering had interacted with the von Liebig Center (Weeks, 2006b). In a study by Gulbranson and Audretsch (2008), 66 projects were funded and 16 companies were spun off from the center’s support by November of 2007. Rosibel Ochoa (interview), director of the center, claimed that these approaches have contributed to heightening awareness of intellectual property among academic researchers. Steve Flaim (interview) also observed that "there was a need for faculty to understand how to protect their intellectual property and how to make it attractive to commercial entities." Flaim described how the program helped faculty understand the development process:

> Faculty were intrigued with the idea of the center. They came to us and told about discoveries they had made and published. They were saying “here is a great technology and I published two years ago in a science journal. Let's make it into a company.” The faculty at that stage were very naïve about how to be entrepreneurs, how to protect technologies. What we've done over the eight years since we've been existent, the School of Engineering became very aware of what's required to protect technology, to make the technology move forward as a company or as a licensable opportunity. (interview)

Specifically, the change is most significant to a group of faculty members who do research having commercial implications, but lack experience and relationship necessary to embark on commercializing activity on their own. Barrow explained why these faculty members have difficulties in transferring technologies: they "don't know how to talk to nor how to find venture capitalists; they don't know about running a company, work procedures, or jargon" (Abigail Barrow, interview). Michael Krupp (interview), an adviser at the center, said of this problem: “they (academic researchers) know what they want to try to do, but they really don’t know how to do it.” The center is located on campus staffed with experienced entrepreneurs who are willing and able to give advice to academics. William Fenical, who is in process of forming a company with the help of the von Liebig Center, has been learning skills and knowledge by participating in the process. He (interview) said of his learning experience by participating commercializing activities with support of the von Liebig Center: "we are starting a company within the university and working with our own university to develop financial and business expertise." His team has been applying funding for early stage development including the UC Discovery Program, the SBIR program and the STTR program. Overall, the center has been instrumental in enabling and encouraging the university people to engage in development activity.

While the School of Engineering focused on enhancing partnerships with industry, the efforts at the School of Medicine revolved around the concept of 'translational medicine'. One of the initiatives to facilitate applications of biomedical research was to launch the UCSD Translational Medicine Program in 2001. The idea of creating the program came from Edward Holmes, dean of the Medical School, to fill the 'translational gap'. Holmes, who had joined UCSD in 2000, steered institutional efforts to bridge laboratory research with medical treatments by instituting a set of programs. The program was launched as a partnership initiative of the School of Medicine, CONNECT, the Technology Transfer Office and a local venture capital firm, Forward Ventures (Somers, 2003).

The basic idea of the Translational Medicine Program was to attract venture capital funding to projects that were too advanced for federal funding but not mature enough to draw attention from private investors. The mechanism was to give academic researchers a presenting opportunity to a group of venture capitalists. Based on commercial merit, venture capitalists chose research projects to infuse funding for further development. But the program's exclusive partnership with a single venture firm was criticized by the local biotechnology community. Facing the critics, the school opened the door to any investors by disclosing research proposals on a website, so any investors could participate (Bigelow, 2002). Unfortunately, the driving force of the program withered as its founder, Edward Holmes, left UCSD to Singapore in 2006.

Another notable undertaking was a formation of a consortium, called PharmStart, in partnership with the University of California, San Francisco (UCSF), Stanford University and SRI International, a non-profit research institute. In this consortium, SRI International, which has expertise and facilities for drug discovery, helps academic scientists set up clinical trials, write business plans and secure funding from government or private investors. SRI International provides industrial expertise combined with lab facilities in brining discoveries to more a commercially exploitable stage. At UCSD, Thomas Kipps, a cancer immunologist who was involved in creating the consortium, described the significance of such a bridging organization: "The area between basic research and [moving drugs into] the clinic is no-man's land. There are lots of mine fields to navigate and it takes a lot of infrastructure and a road map so we don't get destroyed in the process" (Webb, 2003b).

Recently, UCSD launched an institution for supporting and stimulating translational medicine, the Clinical and Translational Research Institute (CTRI). The institute provides resources and infrastructure to do clinical research as well as education programs and funding for translational research projects. In 2010, the institution received a $32 million, five-year grant from the NIH’s Clinical and Translational Science Awards program, which aims to build a national consortium of about 60 institutions. The NIH program intends to build infrastructure to promote practical applications of medical research by enabling researchers to access facilities, tools and expertise.

Along with these institutional arrangements, the university and the local community have created a set of programs, institutions and initiatives as platforms for interactions and communication. Since 2005, the local business and research communities have been collaborating to build an R&D base for stem cell research. The endeavors resulted in the founding of the Sanford Consortium for Regenerative Medicine. In 2006, a group of students at UCSD started a year-round business plan competition, UCSD Entrepreneur Challenge, with an objective of igniting entrepreneurship among students. Through this process, participants are linked to the local business community and learn the skills to start companies. In 2009, local research institutions, including UCSD and TSRI along with the local biofuel companies, formed the San Diego Center for Algae Biotechnology to combine research capacity. These programs and centers, along with programs at UCSD and local associations like CONNECT and BIOCOM, have provided academics venues for interactions with and exposures to entrepreneurial activity.

### 6-4. Development of Practices at Non-Profit Research Institutions

While the University of California has instituted rules on conflict-of-interest and conflict-of-commitment in response to public concern and criticism, non-profit research institutions have rarely received public attention with regard to their commercialization activity. There is no central system of regulating relations with industry by the federal government, but the NIH requires research organizations receiving federal grants to establish and enforce regulations on conflict-of-interest. The NIH oversees policies and practices of federally-funded institutions, and intervenes to preserve the integrity of academic research. TSRI, for example, issued a policy titled 'the Conflicts of Interest and Commitment'. In accordance with the policy, the institution's employees are required to report their outside activity, engagements and financial interest. The rule allows its full-time faculty to spend ten percent of their professional effort on outside work. Even though the principles and mechanisms of the system are similar to those of the University of California, procedures and review process give more discretion and encouragement to their faculty (Scott Forrest, interview). Rolf Muller, who is a cofounder of a biotechnology company (Biomatrica) and used to be director of Assay Development and High Throughput at TSRI, observed the current institutional environment related to participation in commercialization activity:

> TSRI and the Salk Institute all have very liberal ways for their faculty members to move between or have appointments in industry. Each one is very good at supporting technology transfer. It's worthy for scientists to either build companies or support companies through consultancy agreement or being part of the company development. (interview)

As new institutions with virtually no endowment or student-base, non-profit research institutions have adopted a variety of practices of technology transfer to complement their research funding from federal agencies. Frank Dixon, then president of Scripps Clinic and Research Foundation, made a partnership contract with Johnson & Johnson in 1982. Dixon had decided to steer the institution into molecular biology, but he could not find any funding to construct facilities. At that point, the institution, Baskin (1991, p. 253) wrote, "subsisted almost entirely on NIH funds and pursued research mostly on immunology." An agreement with Johnson & Johnson in 1982 brought in about $30 million as grants, contributions and patenting costs in exchange of 'first rights of refusal' for licensing health related discoveries (Kenney, 1986) . In 1985, the institution reached another agreement with PPG Industries–formerly Pittsburgh Plate Glass–around research on pesticides.

At the end of 1992, TSRI announced that it signed a contract with Sandoz Pharmaceuticals, a subsidiary of a Swiss pharmaceutical company. According to the agreement, TSRI was supposed to receive $300 million in return for giving rights of first refusal to inventions to the company for the next ten years. This agreement came under criticism from the Congress and the NIH (Hilts, 1993; Rose, 1993b). Bernadine Healy, director of the NIH, claimed the agreement was not in accordance with the Bayh-Dole Act of 1980: "the Bayh-Dole is a public interest law and what serves the public, not necessarily what serves the interest of a Swiss pharmaceutical firm or a particular institution" (Rose, 1993a). Healy also raised concerns that "it makes Scripps almost a subsidiary or an industrial laboratory of Scripps." In 1994, TSRI had to revise the agreement so that Sandoz Pharmaceutical could license only part of the institute's discoveries. To date, the institution has been partnering with Pfizer under a similar contract.

Comprehensive agreements with large pharmaceutical companies have been adopted by some of the neighboring research institutions largely as a way to enrich their research funding. In return for giving early access and licensing rights to pharmaceutical companies, the research institutions secure funding. The La Jolla Institute for Allergy & Immunology moved into a research park at UCSD in 2006 under the auspices of Gemini Science, a wholly owned subsidiary of Japan's Kirin Brewery company. Gemini Science promised to supplement about 18 percent of the institute's budget in exchange for the rights of first refusal to discoveries and technologies coming out of the institute (Crabtree, 2005a). The Salk Institute established a collaborating program with Sanofi-Aventis, a France-based global pharmaceutical company, which provides research funding to selected projects proposed by Salk scientists and owns the exclusive rights to discoveries from sponsored projects (Somers, 2009b).

Besides partnerships with large companies, the Salk Institute and the Sanford-Burnham Institute have a long history of spinning off their research discoveries. In 1981, the Salk Institute established Institute Biotechnology/Industrial Associates, Inc. (SIBIA) as its privately owned entity. Frederic de Hoffman, then president of the Salk Institute and who was also founder of SIBIA, wanted to capitalize on the institute's research capacity to earn revenues (Fikes, 1993d). From 1988, it started to focus on developing therapeutics by leveraging its exclusive rights to licensing in the field of neuroscience (Fikes, 1993b). The Sanford-Burnham Institute utilized a start-up company, Telios Pharmaceuticals, which had been founded based on a discovery from the institution in 1987, as a commercialization partner. The institution granted licensing rights to Telios Pharmaceuticals in exchange for owning a portion of the company's equity (Fikes, 1993a).

More recently, non-profit research institutions have been investing in building capacity for translational research. One of the underlying reasons that TSRI and the Sanford-Burnham Institute have been so successful is their efforts to stimulate inter-disciplinary research and build capability of drug discovery–to be more specific, TSRI's emphasis on chemistry and structural biology gave it a competitive edge in doing translational research (Baskin, 1991). The Sanford-Burnham Institute, as Paul Laikind (interview), who is vice president of business development pointed out, "invested heavily over last a few years building up its core facilities that allow us to do some of the translation." Due to these investments, the Sanford-Burnham Institute and TSRI were granted a $98 million and an $80 million contract from the NIH, respectively, as part of a project called the Molecular Libraries Probe Production Centers Network (MLPCN), in 2008: the institutions were designated as two of four national comprehensive small-molecule screening and discovery centers by the NIH (Somers, 2008b).

Besides their investments in facilities, local research institutions focus on bringing in people from industry. John Reed (2009), CEO of the Sanford-Burnham Institute, said of this approach:

> One of the paradigm shifts you can see here is that the repatriation of people from industry jobs back in academia interacting with academic scientists to provide the expertise needed to do this kind of things [translational research]. It's really a nice blend of the best of both worlds bringing core competencies and discipline of corporate, for-profit industry together with activity and innovation of non-profit.

During 2009, the institution scouted Paul Laikind, former CEO of a series of biotechnology companies, as vice president of business development, and Michael Jackson, director of a drug discovery division at J&J Pharmaceutical Research and

Development, as vice president of drug discovery and development. Along with these efforts, both TSRI and the Sanford-Burnham Institute have been building capacity in commercializing discoveries either by establishing start-ups or collaborating with established companies. Activity and ability revolves around identifying, evaluating, patenting research discoveries, and licensing out technologies to industry partners, or supporting their scientists to launch start-ups. One of the efforts is to "build a long-term relationship" with business community and to keep robust communications with their scientists (Scott Forrest, interview).

In sum, the local research institutions have developed and adopted practices in a way that facilitate interactions with industry to capitalize on their intellectual base to secure more research funding and, as a result, to strengthen their research capacity. First of all, the development of the practices was the product of polices and institutions of the federal government, including the Bayl-Dole Act of 1980, the emphasis on translational medicine by the NIH, and the SBIR program. The growth of the local biotechnology industry has also been influential to these institutions.

### 6-5. Building Understanding and Relationships

At an individual level, how do academic scientists experience and practice commercialization of their research discoveries or expertise? How have they incorporated the regulations and culture into their daily interactions with industry? In the end, it is individual scientists who initiate or participate in efforts to develop applications. Even though rules and resources have been constituted by the federal government and universities, academic scientists are the ones who apply the given structures in their daily lives through their actions and interpretations. In this regard, it is the attitude, interest, motivation and experience of individuals that is most crucial in turning inventions into innovations. Denise Lew (interview), a senior licensing officer at UCSD, claimed that "if faculty are not interested in working with industry, there isn't any tool forcing them." Academic researchers have a duty to disclose their inventions, but discretion about whether to cooperate in their commercialization.

Asked if UCSD and research institutions in San Diego were entrepreneurial, David Kabakoff, a venture capitalist, who also has founded several start-ups, responded by pointing to academics who had engaged in entrepreneurial activity: the major positive impact factor, in words of Kabakoff (interview), is "the faculty members," even though there are technology transfer offices and facilitators because "it is really the initiative, track record, confidence and leadership of individual faculty or researchers." To the local community, Irwin Jacobs, founder of Linkabit and Qualcomm, and Ivor Royston, founder of Hybritech and IDEC Pharmaceuticals, are a symbol of academic entrepreneurship. Jonas Salk, founder of the Salk Institute, founded a start-up to develop an AIDS vaccine in 1986 and was committed to this endeavor to his death. Even though the company failed to produce any treatment, it was "a well funded serious entrepreneurial effort", which helped construct the collective memory of the local community (Kabakoff, interview).

An entrepreneur, John Stuelpnagel, who had formed Illumina with academic scientists, also argued that the extent of commercialization of university research depends critically on the 'people factor':

> I think it really comes from the academic person, who is emotionally involved in technology, wants to see it commercialized and is willing to put significant amount of energy into that effort as opposed to his academic lab. (interview)

Therefore, a great deal of technology “just sit” at universities if the university licensing offices “are so difficult to deal with, they want to keep control of it or they are not very articulate” (Larry Bock, interview). Regarding the importance of communication capacity of academic inventors, Bock observed:

> There is a lot of scientific stuff going on at any one point of time, but not every single bit of it is getting commercialized. The stuff that is getting commercialized is important stuff, but also because it has somebody who can tell you why it is important. (interview)

The influence of entrepreneurial colleagues on stimulating academics to venture into commercializing endeavors is well illustrated in an account by Dr. Floyd Bloom, chairman of the Department of Neuropharmacology at TSRI and also editor-in-chief of the journal Science. He cofounded a biotechnology company, Neurome, in 2000 to commercially develop his research. As shown, he ascribed his full commitment to his venture to predecessors:

> The examples of other faculty who have gone from academia into biotechnology inspire those of us who haven't done it to try to take a chance, [to] enter the marketplace, find financial support. I could probably have let someone else run with it, but I don't know how many more swings at the plate I have. So, I wanted to run with it myself (Crabtree, 2000).

The successes of colleagues encourage scientists to think about commercialization of their laboratory projects, and the predecessors empower them to deliver by providing guidance and networks.

Motivation and interest in commercialization largely depend on the inventors' stock of knowledge, depth of experience and extent of social interactions. Academic scientists, according to Kleanthis Xanthopoulos (interview), become motivated and take actions when they "understand that process, the real value of invention in creating a company or in developing a drug." Therefore, if academic scientists have a greater appreciation of the process of commercialization, they are more likely to engage in commercializing activity and succeed in mobilizing resources.

In addition, the success of finding partners from industry depends largely on interactions and relationships between academic inventors and industry. Denise Lew described the importance of the interactions:

> Really our best source of getting licenses out is directly from the investigators because they are going out and talking about their work… We always need cooperation from the faculty again. If they know of companies that are interested or could be interested, those are the ones that we want to contact, especially if they have a personal contact at the company. (interview)

This account echoes a claim of Jane Moores (interview), Assistant Vice-Chancellor of Technology Transfer Office at UCSD: it is interactions between inventors and people from industry that lead to "the most productive relationships" for reaching licensing agreements. Regarding the importance of relationships and mutual trust between academic researchers and scientists from industry or entrepreneurs, Michael Krupp (interview), an adviser at the von Liebig Center, explained: “it is really quite rare that a company comes in the technology transfer office saying ‘I want to license that technology’ and then walks away with the technology.” Michael Rondelli, director of the technology transfer office at San Diego State University, also emphasized the importance of relationships between faculty inventors and entrepreneurs, who bring in “an incredible amount of skills” to commercialize technologies by establishing start-ups:

> You can't start a company just by walking in and having an hour meeting. It takes a long time; it takes many meetings; and even faculty have to see for a long time how they [entrepreneurs] work through challenges and how they work through opportunities before faculty can really say 'this is someone who I want to partner with.' That's the problem that every tech transfer office is struggling with. [But] it is valuable because that struggles, I think, actually create the good relationships. (interview)

Although companies enter into a licensing contract with universities, the legal agreement is a byproduct of long-term collaborations and communication between academic and industrial laboratories. Thus, technology transfer, Michael Krupp (interview) argued, revolves around “almost always collaboration between a laboratory and a group at a company.” In this respect, one of the most important and challenging roles of the technology transfer office, Michael Rondelli (interview) explained, is to learn “how to mash the personality in our faculty with the personality of the potential entrepreneur and how to make them work together as well as to pick the right people.”

In addition to the above avenues, academic scientists’ experience and interactions influence technology transfer activity through social reputation. As academic scientists engage in commercialization activity, they develop not only expertise, skills and relations, but also reputation as a scientific authority. Venture investors and established companies prefer to collaborate with academic investigators who have been involved in commercializing basic research. As Scott Forrest (interview), director of the Office of Technology Development at TSRI, noted: "people who have done before don't have a problem. The venture capitalists want to find them and want to interact with them because of their attractive track record."

The case of William Fenical, director of the Center for Marine Biotechnology and Biomedicine at the Scripps Institution of Oceanography, illustrates how an academic scientist becomes competent and motivated in developing applications. Following ten years of research, Fenical decided to develop drugs from marine organisms. He and his team focused on developing compounds having anti-inflammatory effect in the early 1980s. Within one year, they succeeded in drawing attention from existing companies and licensing their discovery to one of those companies in 1985. This was his first experience of turning laboratory research into a product through licensing contracts. Fenical (interview) said, "it was a product that we felt proved the principle that we had been speaking out: there are compounds in the ocean, produced by marine life that have commercial importance in pharmaceuticals, cosmetics and agricultural."

Soon he turned his focus to marine microbes. His team developed techniques and expertise in collecting, isolating and cultivating microorganisms that live in deep ocean sediment. They discovered several compounds with antibiotic and anticancer properties (Marris, 2006). But, at this time, no pharmaceutical companies were willing to license and develop the compounds. They continued to report their discoveries to the Technology

Transfer Office at UCSD. The office asked them to find partners who would license their disclosed discoveries and pay patenting costs. Unable to bringing in any partners from industry, they were "stuck with no way to proceed" (interview). At this point, a member of staff at the Technology Transfer Office of UCSD approached Fenical and his team to help them find venture investors. In 1998, Fenical with colleagues founded a biotechnology firm, Nereus Pharmaceuticals, to develop cancer drugs based on investments from a local venture capital firm, Forward Ventures. The venture capital firm brought in a seasoned entrepreneur, and Fenical shifted his involvement with the company as consultant (Webb, 2001). Fenical's team helped the company acquire their research expertise through demonstration and training.

Around 2006, he embarked on another endeavor to find and develop antibiotics from sediment of ocean. This time, he and his team were well aware of how to attract the attention from the investors' and entrepreneurs' community by virtue of previous experiences. They formed an interdisciplinary team of medicine, pharmacology, chemistry, and biochemistry, who, as a team, knew "after many years of experience what a drug looks like, what properties it needs to have and what attracts attention" (interview). Then, they began to inform their plan and to raise awareness of the local biotechnology community by giving presentations to local trade groups, biotech companies and foundations (Weeks, 2006c). Instead of licensing to established companies or partnering with venture capital firms, they chose to create a company by themselves with the help of the von Liebig Center. To conduct the early stage clinical development, the company has been seeking funding from the UC Discovery Program, the SBIR program and the STTR program. By drawing on these management and founding sources, Fenical (interview) said, in about three years, the company would advance the technologies and would "be positioned in such a way that it will be appealing" to existing companies or investors. Through the experience from academic research and interactions with industry, Fenical has acquired know-how to transfer technology as well as acumen in drug discovery from multiple disciplines.

Gary Firestein, who is currently heading the center of Translational Medicine at UCSD, exemplifies how experience in industry can critically enrich understanding, perspective and skill sets necessary to collaborate with industry. He has been a laboratory investigator studying the pathogenesis of rheumatoid arthritis. He became an assistant professor of medicine at UCSD in 1988. In 1992, he joined Gensia Pharmaceuticals, a local biotechnology company, to head their immunology program, and he stayed at the company for five years until he returned to UCSD (Webb, 2002b). At Gensia Pharmaceuticals, he had learned three skill sets that he applied not only to his research but also fundraising and directing programs at UCSD established to facilitate translational research: first, he acquired "management and strategic planning experience" by directing a department; second, he experienced and learned the process of drug discovery which begins "with identifying a target, developing compounds, doing toxicology, developing assays by working with chemists and academic collaborators (interview); third, he also learned how to do in-vivo studies by working at Gensia Pharmaceuticals.

Most of all, by working in the industrial setting, he (interview) learned "how to set up successful collaborations with industry." When he returned to UCSD, he knew what industry scientists would want from their academic partners, in addition to insights and understanding on the entire process of drug discovery. He chose to commercialize research discoveries by collaborating with established companies rather than to found start-ups because the latter activity would require too much commitment. Since then, he has been active in developing better therapeutics for rheumatoid arthritis through doing academic research, consulting and advising companies and leading translational research programs at UCSD. Firestein (interview) said that faculty having working experience in industry "adds something to the environment to have an appreciation, a detailed appreciation of what and how the private sector actually works."

The case of Michael Heller, professor of nanoengineering and bioengineering at UCSD, also is an interesting example showing the importance of industry experience in transferring knowledge. In 2001, Heller (interview) joined the School of Engineering to "go back basic research that we can't really do at a company." In the early 1980s, he started working at a start-up company that focused on developing diagnostics based on DNA probe technology. After participating in creating and managing another biotechnology company in Iowa, he came to California. At this time point, he chose to be an independent scientist studying microarray technology for two years. In 1990, he cofounded a biotechnology company, Nanogen, to develop microarray technology for gene sequencing. He joined faculty of UCSD in around 2000.

At his laboratory at UCSD, Heller has been focusing mostly on projects that can lead to applications within five years. Recently, he has been involved in helping one of his graduate students, Raj Krishnan, found a biotechnology start-up, Biological Dynamics. The support and advice from Heller, Krishnan mentioned, were instrumental in pursuing entrepreneurial endeavor. Krishnan (interview) said: "you have to have the support from somebody who has done this before. We could not have done what we have done without Dr. Heller." Heller told that he was proud of Krishnan who had been undertaking the entrepreneurial endeavor. Most of all, Heller, as a faculty adviser, gave "them [Krishnan and his colleagues, who founded Biological Dynamics] a lot of freedom to do things" because that was what he wanted them to do. Second, he gave guidance on business and introduced Krishnan to the venture capitalists with whom he had worked. He described his capability in this way: "I worked in a very big company, I worked in start-up biotechnology companies, I started biotechnology companies, and I've been at the university. So, I can see the whole spectrum of what is necessary to move research to development and commercialization."

The case of Dennis Carson, director of Moores Cancer Cancer at UCSD, provides another example highlighting the role of experience and expertise in translating medical research to applications. In the late 1970s, he synthesized nearly 25 compounds to treat cancer in his laboratory when he was at Scripps Clinic & Research Foundation (Sleeper, 2003). He (interview) went through "all the process from synthesis to clinical trials" with one of the compounds. It was approved by the FDA in 1993 – the compound is prescribed as Leustatin – and became a standard treatment for hairy cell leukemia, a rare kind of cancer (Crabtree, 2006b).

As the biotechnology industry started to develop in California, Carson "took this experience and worked with venture capitalists." From the beginning, venture capitalists came to him to identify any inventions from an “experienced researcher.” Since then, he has been a scientific founder of six biotechnology companies – five of them were founded in San Diego. He (interview) explained his expertise: "Because I am a physician, I see patients, but I also know how to do organic chemistry, pharmacology and molecular biology." A venture capitalist, Standish Fleming, who worked with Carson, noted why investors like himself count on him:

> The best scientists, like Carson, have an intuitive feel for science and rely on that intuition to follow a thread of research that can lead to new and substantial breakthroughs. But not many have an innate feel for commercially relevant opportunities, the ability to focus on medically relevant aspects of research that can be brought to bear on treating diseases. (Crabtree, 2006b)

He also learned and developed the acumen necessary to move research into products and processes. Wendy Johnson, who worked with Carson at a biotechnology company, Salmedix, attributed the success to his business savvy:

> He is very successful because he knows how a small company works. Most academic people have this idea [basic research], but they really have no idea of how to get from this point to that point or what investors want to see. Dennis knows how to do that. He knows what kind of data should be generated in order to get a patent because he understands intellectual property. He knows what investors look for.

Faculty members who have participated in or experienced commercializing activity, either in-person or indirectly, tend to be supportive of entrepreneurial endeavors by their students or postdoctoral fellows. Rather than discouraging or resenting such interests, these primary investigators are more likely to encourage and enable their students to engage with industry. The existence of a group of faculty members favorable to academic entrepreneurism has an effect on cultivating the attitude and ability of young talent. In the process of launching a start-up, Krishnan (interview), who had established a biotechnology company, "knocked the door of faculty, Dr. Heller, Dr. Esener, Dr. Carson and Dr. Shu Chien, who helped along the way." Participation of renowned scientists is crucial in elevating credibility and visibility of early-stage companies.

Dennis Carson (interview), director of Moores Cancer Cancer at UCSD, explained how he helps young scientists seeking his assistance: "I review their executive summary of business plan, I also call up potential investors or CEOs for them" because young people should work with very experienced people. He emphasized the need for collaborating with professionals from various fields to successfully commercialize basic research:

> They need to work with a very senior person like me, or like David Kabakoff. They can't do it by themselves. They have to work with somebody who knows the technology transfer people, who knows the investors, who knows the lawyers. You can't do by yourself. (interview)

Philip Low, founding CEO of NeuroVigil, established a start-up to commercialize his doctoral research at the Salk Institute. Building on his experience, he gave an insider's perspective on the impact of 'entrepreneurial faculty' in nurturing and nourishing academic entrepreneurism:

> We see people that we respect work in companies, they found companies. It's not viewed as a discredit, it's not viewed as a bad thing; quite the contrary. If you are a scientist doing revolutionary research and you create a company around you, people

> say, 'wow, this is good.' This is part of the culture. In terms of the process, usually what happens is that your Ph.D. adviser will say when he meets someone, 'my student has created this. We are looking for investors.' And he will talk to other scientists who founded companies, who know investors, investors will come and meet you and your Ph.D. adviser. (interview)

He continued to say that it would have been impossible for him to launch a start-up if he had done his Ph.D. or post doctoral research in other places. There, his adviser might have ordered him to focus only on research projects, not allowing him to explore ventures for commercial development:

> If I had been a graduate student in another place, my Ph.D. adviser would never have let me have the freedom to travel around the world saying 'you have to just complete this project. We submit this and that's it. If you want to be in industry, then you do the industry thing, but you don't stay at my lab.' Here, they [faculty] understand because they had created companies before. (interview)

In a case of Peter Kuhn, an associate professor of TSRI, interactions with industry are a critical avenue to educate his students and himself. He said of the importance of interactions with industry:

> We have to train our students to learn how to deal with that reality. So, we have to train our students for the academic path, but also for the industrial path. Therefore, they have to understand what it means to work in the industry, and the easiest way to understand is interacting with scientists in the industry. (interview)

At the same time, collaboration with industry helps him know "whether the work fills a particular unmet clinical need and whether a partner is out there." When he moved to San Diego from Stanford University, he with three colleagues organized a group, called Shout, which consists of about, in his words, 35 “young movers and shakers” in academics, industry and venture capital. They have been holding meetings every four months. In addition to these motivations, the physical proximity and the openness of the

San Diego biotechnology community are also significant factors facilitating interactions with partners both in academia and industry. Kuhn described his learning experience through engaging in the local community:

> In such an open community, you gain understanding of that [whether the work that you do fills a particular unmet clinical need and whether a partner is out there with whom you can work], not by reading textbooks, but by talking with people in industry – biotechnology or pharmaceutical – by talking to lawyers, bankers and all kinds of people… Without that education, I would not drive the research programs the same way. You might end up with solutions to problems that don't exist. (interview)

Experience in collaborations provided a critical stepping stone for building more productive partnerships. Collaborations involve definitions of roles, approaches to solving problems and channels of communications between participants. To make progress, the partners should "figure out how to formalize collaboration" (Peter, 2009). He continued to mention how he had learned to collaborate with academic and industry partners: "If you find a sweet spot of how to work with people, then that really works." Through experience, he learned to formulate and run collaborative partnerships in a more productive way:

> If you do it once, you learn a lot. But if you do it two or three or four times, you will be getting better and better at it and you build up your network of people you work with. (interview)

The academic researchers, who interviewed for this dissertation, learned to enact regulatory and supporting programs, and formulate collaborative initiatives through doing and interacting. Knowledge and relationships nurtured by participation and engagement form the ground not only for individuals' entrepreneurial activity but also for the culture of research institutions. By the same token, experience and practice of academic researchers are critical in constituting the regulating framework on technology transfer.

Academics having experience in and relations with industry are well positioned to deal with regulations on interactions with industry. Most academic scientists see the regulations, as “a necessary evil” to protect the environment of academia, but it also produces paperwork and bureaucracy (Scott Forrest, interview). To address the regulatory hindrance, academic scientists need to understand any potential conflict-of-interest or conflict-of-commitment prior to their engagements. The understanding and practices also come through hands-on experience and participation in communities.

Gary Firestein (interview) explained the importance of understanding of regulations in interacting with industries: "understanding what potential conflicts are versus real conflicts, understanding how that influences behavior and interpretation is very important in assessing these interactions." As a way of developing technologies, he has consciously chosen to license out inventions to existing companies rather than form a start-up. He adopted this practice to minimize his commitment to activity outside of the university. William Fenical took an opposite direction in developing therapeutics. As noted, recently he and his team chose to create a start-up on their own to pursue their development efforts. Although paperwork and procedures required by the regulations on conflict-of-interest take his time, it is not a significant obstacle to him, as he described:

> Fortunately for me, I had served on this [conflict-of-interest] committee prior to being the subject of its oversight. I knew the rules, I knew what should be done, I knew how to behave, I knew the process. (interview)

Dennis Carson described the role of experience in working with staff of the UCSD Technology Transfer Office:

> If one is experienced, and has inventions that made money for the university, then the guidelines are much easier to work with because they trust you... Its barrier to entry is very high, but once the barrier is completed, and you succeed, then it's not that hard. The hardest for me is the initial barrier to entry. (interview)

To avoid any violations, he has enacted and adhered to a principle that he would end his engagement with co-founded companies before they go public or enter into Phase II clinical trials (Sleeper, 2003).

As these episodes illustrate, meaning and properties of regulatory schemes are created and enacted by individuals' interactions and involvement. Academic scientists who have participated in commercialization activity develop knowledge and practices in the process of doing and interacting to deal with problems. Academics have developed a certain type of perspective and insights into academic entrepreneurism in process of interacting with colleagues and taking actions to deal with problems. The University of California has constituted rules and policies to either constrain or enable entrepreneurial activity of their employees. The programs introduced by the federal government and UCSD have contributed to bridging gaps in resources and skills. However, the patterns of interactions between academics and entrepreneurs, and the attitudes of academic scientists toward participation in entrepreneurial activity are rooted in the daily interactions and social lives in communities.

Not all academic researchers at UCSD and local non-profit research institutions are comfortable and competent with technology transfer; UCSD has not developed the most supportive system for academic entrepreneurship. Yet, a large part of faculty at the School of Engineering and Medicine has become familiar and comfortable with interactions and relationships with industry. Non-profit research institutions have developed their practices and resource base to promote development of medical applications. Brook Byers, venture capitalist who co-founded Hybritech, described relationships between academic institutions and industry in San Diego:

> After the Hybritech start-up, I went on to help another dozen companies get started and grow in San Diego. The San Diego community has a more cohesive characteristic compared to Silicon Valley, Austin, Cambridge, Seattle, etc. There is something special about how UCSD, Scripps, Salk, etc. work together with the business community. (Fikes, 1999)

In 1993, an industry scientist, Gertt Caspritz of a German pharmaceutical firm, was impressed by the rigorous interactions between academic researchers and people from industry during his trip to San Diego. He noted:

> What is striking is how closely university people work together with biotech start-ups. It is my personal impression that the close interaction between industry and science, the almost daily interaction, drives the process forward. (Fikes, 1993b)

He added that such interactions would be infeasible in Europe because they "would qualify as a clear, classic conflict-of-interest" (Fikes, 1993b). Joseph Panetta, CEO of BIOCOM, attributed the daily interactions to the geographical proximity between institutions and companies:

> UCSD, Salk, Scripps, Burnham, Venter Institute, La Jolla Institute, all of those are right in the middle of the biotech industry, surrounded by all the companies. Literally, across the street are all these companies... The reason that we've got this environment where scientists and industry interact so closely is just because we are right there next to each other. All the time, we see each other. (interview)

As they live and work next to each other, there is a constant flow of interactions back and forth. Peter Kuhn (interview), a professor of TSRI, also attributed the robustness of interactions to spatial closeness. Every academic scientist can reach to any partners at neighboring research institutions or related companies within ten minutes either by walking or driving: "everybody is physically so close." In San Diego, in words Gary Firestein’s words (interview), a professor of UCSD, academic scientists are "surrounded by hundreds of biotechnology companies."

Along with spatial closeness, research institutions, including UCSD, and trade associations like CONNECT and BIOCOM are another important factor which fostered the interactions. Irwin Jacobs, founder of Qualcomm, explained the role of UCSD:

> Many of us came out of the university [UCSD] and used to talk to a lot of colleagues. We didn't come out of a business setting. That was a positive aspect to it. Secondly, physically, a lot of companies were centered very closely to UCSD and came to lectures at UCSD or set up lectures ourselves and invited others. So, it just became a very positive aspect of stimulating communication. (interview)

UCSD and trade associations organize a series of meetings in forms of lecture, workshop, forum, symposium, panel discussion and network event every year. The events or programs held by these community organizations provide another venue for learning and networking. For example, the Moores Cancer Center at UCSD holds an annual symposium, called the Moores UCSD Cancer Center Translational Oncology Symposium. To academic researchers, the symposium is a space for presenting novel discoveries to people from industry and academia. Dennis Carson (interview) said of the impact of this event: "We get hundreds of people from industry and universities. They come together and talk to each other". And most of all, at these meetings, "very experienced people meet young people."

CONNECT has held a lecture series, Frontier in Science and Technology, virtually every month, where academic researchers present their up-to-date discoveries. To facilitate communication between leaders from industry and academia, CONNECT started a networking event – the Annual La Jolla Research & Innovation Summit – in 2009. To researchers looking for ways to create a start-up, business competitions are a venue to educate themselves. The San Diego Tech Coast Angels and a student organization at UCSD both established platforms that train scientists to formulate business plans and pitch them to the public: Annual Quick Pitch Competition and the UC San Diego Entrepreneur Challenge, respectively. Scientists without much experience learn not only by participating in the programs but also attending as audience. Besides these meetings, a number of institutions and associations have events and programs related to their own respective missions.

Programs and groups like CONNECT, the San Diego Tech Coast Angels and local venture capital firms help stimulate academic entrepreneurship by creating education and resourcing opportunities for academics. In Joseph Panetta's (interview) words, the San Diego biotechnology community has "all kinds of courses outside of university that give things like business skills and presentation skills." Academics can utilize the von Liebig Center, the Springboard program at CONNECT, the San Diego Tech Coast Angels and the local venture capital community when they pursue to create start-ups or help companies develop commercial applications. Stephen Flaim (interview), an adviser at the von Liebig Center, referred to the various and linked programs and events that help academic scientists venture into the entrepreneurial world as “an ecosystem of innovation.”

In summary, the patterns of academia-industry relationships in San Diego have unfolded through actions and interactions of individuals. By being involved in entrepreneurial activity and with entrepreneurs, academics developed attitudes toward and practices for technology transfer. They not only learn the skills and expertise for commercialization activity, but also develop the practices necessary to deal with regulations and potential conflicts. In this sense, the patterns of interactions in the San Diego biotechnology community have their root in its geographical proximity, and are nurtured by educational and supporting programs within and outside academic institutions, which have fostered hands-on experience and face-to-face interactions.

# CHAPTER 7: THEORETICAL AND POLICY IMPLICATIONS

The objective of this study is to understand the localization of industry and the translation of academic research into entrepreneurial activity by investigating the historical evolution of the biotechnology cluster in San Diego. I found that day-to-day practices and interactions in communities have deepened and broadened the capacities of multiplying start-ups and commercializing academic research. By engaging with people and problems at start-up companies and within circles of friends, participants have developed the skills and expertise to be entrepreneurs or entrepreneurial scientists. In the process of solving daily problems through discussions and engagements in their communities, participants have developed their knowledge and practices, which have fueled the entrepreneurship and innovation of the San Diego biotechnology community. Therefore, the learning and interacting experiences within communities are the engine of the development of the San Diego biotechnology cluster, and the basis for the relationship between academia and industry. In other words, it is the human process, in which understanding and solutions emerge and spread.

I found that the formation and flourishing of the biotechnology cluster in San Diego is rooted in a dynamic environment of learning and engaging: (1) a mass of start-ups and small companies, which enabled and, in some sense, forced employees to learn the entire process of biotechnology business; (2) constant inflows of talent from outside San Diego, which complemented and supplemented the local knowledge stock and practices; and (3) networking and communicating opportunities, provided by trade associations and research institutions. These three factors have critically fostered individuals' learning process by facilitating the formations of communities for learning, enabling individuals to participate in communities and promoting interactions between communities. In sum, the emergence of the San Diego biotechnology community was the process of creating and circulating local knowledge and practices in multiple communities.

In this chapter, I discuss my findings in relation to the literature on industrial clusters and technology transfer. Then, I explore the significance of this study to theories on structuration, resourcing and social learning. In the final section, I suggest lessons for cities, regions and countries interested in stimulating their economies by nurturing biotechnology clusters and capitalizing on research universities.

**7-1. Contributions to the Literature**

This study seeks to contribute to deepening our understanding of industrial clusters, knowledge transfer and entrepreneurship, by drawing on theories about social structuration, situated learning, communities of practice and economic development. In Marshall's (1961[1890]) words, "the mysteries of the trade become no mysteries," in industrial clusters, due to actions and interactions in multiple learning communities. I found that the multiplication and diversification of the localized industry – the San Diego biotechnology cluster – are the consequence of individuals' learning process in communities. Learning takes place as individuals engage with people and problems in their daily lives. In the process, participants absorb, develop and circulate the knowledge, practices and understanding necessary to create and run biotechnology businesses. This is also the process whereby learners become skilled and committed entrepreneurs, who continue to be involved in entrepreneurial activity. Communities for learning emerge, most of all, in companies, where groups of employees lead efforts to solve day-to-day problems to adapt to ever-changing situations and to learn from on-the-job experience, either on their own or as a team. The experience and interactions produce a stock of knowledge, a set of practices and relationships, which enable the participants to scale up and spread entrepreneurial activity. Frequently, they need to reach out for resources or references outside their primary community. The understanding created and circulated within a community spread across multiple communities in the process of interactions and collaborations. The cross-fertilization of ideas and practices contributes to the deepening and widening of skills and expertise. The extent of knowledge and practices spillover is contingent on the spatial and cultural context under which individuals have interactions and engagements.

Since Marshall (1961[1890]) used the term "external economies" to explain the localization of industry, a large body of literature has been devoted to examining the existence and extent of this effect. Several literature review papers have been written to combine empirical studies on the impact of external economies and patterns of industrial agglomerations (e.g. Feser, 1998; Feldman, 2000a; Koo, 2005). Empirical analyses contributed to understanding the sources of externalities and the impact of agglomeration. These studies have contributed to drawing attention to industrial clusters and provided policy guides to national, regional and local governments. However, they rarely discussed what factors account for the robust entrepreneurship and innovation in clusters. Further, these studies provide somewhat limited explanation about the beginning and process of localization of industries, which is epitomized in a remark by Krugman (1991, p. 67): "at ground level there is a striking role for history and accident." A large part of the findings of this research is consistent with the literature, in that engagement and interactions – which account for the proliferation of start-ups and the spread of knowledge – are contingent on geographic proximity and environmental factors. This study also highlights the importance of industrial clusters for fostering entrepreneurship and innovation: a large part of entrepreneurship and innovation originate in the process of interacting and engaging with peers and partners. But this research found that the industrial localization and knowledge spillover are attributable to, most of all, daily practices and interactions in and across communities. In this respect, this study broadens the literature on clusters by suggesting another process or mechanism for localization: learning through participation and interactions.

This research contributes to the literature on local economic development and industrial clusters from economic sociology and urban studies. Jacobs (1970; 1985), Sabel (1982), Saxenian (1994), Brown and Duguid (2000), and Florida (2002) shed light on the significance of human interactions and the dynamic learning process in industrial clusters. These studies attribute economic development or the formation of industrial clusters to social and cultural processes. Particularly, Saxenian's (1994) study was instrumental in broadening our understanding about industrial clusters. Florida (2002) drew further attention to the significance of "the creative process" and "the creative environment" to the local economic prosperity. In line with these studies, this dissertation found the social process is the most important component in the development of the San Diego biotechnology community. However, this research might contribute to expanding the literature by demonstrating how the social and learning process takes place at the individual and group level, and influences individuals, who are the primary agent of economic activity. This study enriches the literature as it explored a case, the San Diego biotechnology industry and its regional economic development, which has not drawn enough scholarly attention.

This study has implications regarding the role of research universities and technology transfer. As discussed in Chapter 2, regarding the role of research universities, the literature gives limited and somewhat inconsistent explanation. To explain the differences in knowledge spillovers between universities, regions or countries, many researchers draw on the tacitness of knowledge and its limited transferability. In this sense, researchers point to 'human factors' to account for the different degrees of impact on local economies between research universities. Zucker and Darby (2006, p. 1) noted, for example, that "the embodied knowledge, insight, taste, and energy of the starts plays a role separate from their potentially disembodied discoveries." Owen-Smith and Powell (2004, p. 197) also ascribed the variations in information spillovers to human factors: "the institutional and legal arrangements that secure directed information transmission are an outcome of participant commitments and efforts."

The limitation of the literature is, in part, because many previous studies regarded knowledge transfer between academia and industry as transactions of goods and services;

we need to recognize that knowledge transfer consists of practices and experience. Knowledge transfer involves, in essence, interactions and shared understanding between academics and entrepreneurs. However, academia is constituted and maintained to serve basic research activity, while industries adopt logics and practices to maximize economic efficiency. As presented in Table 6-2, I suggest that knowledge cannot be automatically transferred because of these differences. Academic scientists must have understanding and be familiar with practices and culture of the industry in order to be successful in transferring knowledge or in commercializing laboratory discoveries. I found that academics gain experience in, and exposure to, entrepreneurial activity through interactions and engagements in their communities. By being embedded in communities of entrepreneurs and investors, laboratory scientists learn to be able (and willing) to appreciate the commercial aspects of their research and to participate in the commercializing process. At the same time, interactions with academic colleagues who have experience in and relationship with industries, give another opportunity to learn about the industry side. Daily interactions and participations in communities create and reformulate rules and resources for knowledge transfer or commercialization of academic research. Therefore, the scope and speed of knowledge transfer are the product of "the situation of social life." (Giddens, 1984, p. 22)

From the perspective of the literature on social structures, practices and organizational learning, this study highlights the significance of concepts, like structuration, resourcing and communities of practice, in explaining the localization of industry and knowledge transfer between academia and industry. Giddens (1979; 1984), Sewell (1992) and Weick

(2001) proposed theoretical frameworks to understand the cause and process of structuration. Built on these concepts, Orlikowski (1992; 2000; 2002) and Feldman (2004) showed how individuals at an organization constitute and reconstitute interpretive schemas and resources through daily actions and interactions. Studies by Lave and Wenger (1991), Orr (1996) and Wenger (1998) provide theoretical concepts – situated learning, narrative activity and communities of practice – to understand how individuals participate in creating and recreating social structures, and, at the same time, how they become embedded in social structures. Particularly, these studies shed light on the critical role of participation and engagement in communities of practice or social situations in learning and enacting social structures. Brown and Duguid (2000a) drew on the concept of communities of practice to explain the rapid spread of knowledge in Silicon Valley, but they limited their focus to suggesting the role of communities of practice for facilitating knowledge circulation. Thus, this dissertation broadens the literature by applying the concepts from organizational studies to understanding entrepreneurship, industrial clusters and knowledge transfer.

I propose that more attention should be paid to the learning process in communities and its impact on spawning 'microclusters'. So far, scholarly attention was given, mostly, to the entire ecosystem of industrial clusters like Silicon Valley, Route 128 or San Diego. However, as this dissertation suggests, each cluster consists of multiple communities, in which participants create and share their knowledge and practices through interactions and engagements in the problem-solving process. The multiplication and diversification of entrepreneurial activity would likely be better understood if we look into how each group of practitioners evolves, how participants of a community communicate and how members from different groups interact. Lohr (2007) reported many ‘microclusters’ in Silicon Valley, which were spawned out of communities like companies, alumni groups, ethnic communities and even weekend sports clubs.

### 7-2. Policy Implications

For many countries and regions, nurturing the biotechnology industry and creating a version of Silicon Valley are their first priority of economic policy. It is a consensus that cultivating their version of Silicon Valley or San Diego will determine their economic prosperity in the coming decades and even centuries. Almost all developed as well as developing countries have initiated their own master plans for nurturing biotechnology clusters. For example, Singapore has been leading efforts to be the *Biopolis of Asia* at the national level (Govindan, 2005). The Netherlands named its biotechnology cluster as Bio-Delta, Switzerland supports the BioAlps and BioValley, and Saudi Arabia has been working to transform one of its cities, Jeddah, into BioCity (Pollack, 2002). At the regional level, according to a survey (Battelle Memorial Institute et al., 2006), all states in the U.S. have taken steps to develop their own biomedical industries. States and local governments commonly initiate strategies or public investments to nurture ‘biotechnology valleys’: Florida committed to investing almost $1 billion to germinate their biomedical industry by attracting non-profit research institutions – most notably, TSRI and the Sanford-Burnham Institute, and North Carolina created the North Carolina Biotech Center.

However, in attempting to nurture a biotechnology industry, promote academia-industry collaboration and invigorate local economic activity, policy makers tend to be mystified: economic issues seem distinct from other community issues. Thus, these economic issues are thought to be addressed by experts from outside who have specialized instruments and techniques. Furthermore, many policy makers and political leaders seek to discover 'recipes' and 'models' that could be implanted or imported. They tend to design and construct resources, for example, by building incubators and by creating public venture funding. In contrast, this study implies that entrepreneurial activity, at least related to the biotechnology industry, and technology transfer activity should be viewed more as human endeavors, which involve commitment and collaboration of multiple participants. Because people learn to be capable at social and cultural activity, regional economic development is the consequence of learning through practices at both the individual and community levels. As Jacobs (1985, p. 140) noted: "development is a do-it-yourself process; for any economy it is either do it yourself or don't develop."

It is within communities where individuals learn to be entrepreneurs or practitioners. Individuals need a social space, where they have daily hands-on experience with ongoing issues and communication with colleagues. The locus of learning involves companies, circles and communities. Individuals produce and accumulate knowledge and practices by situating themselves in these groups. Therefore, policy makers must devote public resources to creating and energizing communities for learning. As discussed in Chapter 5, start-up and small enterprises not only constitute a part of economic activity, but also take a role of educating and training future entrepreneurs. In this sense, start-up and small companies are the locus of innovation and entrepreneurship. These companies create the space for employees and managers to be involved in solving problems, and to spearhead skills and forge identities. These companies are firmly rooted in the local environment, and are the main players of sharing understanding and knowledge. Countries and regions used to heavily invest in physical infrastructure and focus on attracting large corporations, but, San Diego turned into a center of biomedical and telecommunications industries from a 'booms-and-busts' town by giving focus to promoting start-ups and connecting them. The resurgence of San Diego's economy reflects the importance of growing small enterprises and start-ups locally.

A sense of connectedness makes a significant difference, particularly, to newcomers. Employees and students need to engage with groups of seasoned entrepreneurs and experts to absorb the knowledge and practices necessary to be independent entrepreneurs. As described in the previous chapters, academic scientists and employees became biotechnology entrepreneurs by meeting and working with veterans. CONNECT has been instrumental in nurturing the biotechnology cluster because it has focused on constructing a platform for openness and cooperation. The leadership and efforts of CONNECT have enabled and encouraged many seasoned entrepreneurs to interact with newcomers. In addition, CONNECT has been leading efforts to create a distinct culture in San Diego by recognizing and honoring the virtues of entrepreneurs. Most of all, CONNECT is a community-based organization, which is governed by the representatives of the entire community and run, mostly, by volunteers. Through its many programs, veteran entrepreneurs meet young entrepreneurs, and they engage in discussions and workshops.

Since all participants stand on shared interests, values and practices without bureaucratic interference or control, they create a learning and supporting community. The case of the San Diego biotechnology community and CONNECT reflect what Florida (2002, p. xxiii) pointed out: “growing a creative ecosystem is an organic process,” and “the solution lies in the hands of each region – in the knowledge, intelligence and creative capacities of its people.”

Business resources – by which I mean venture capital, angel funding and specialized services – are a crucial factor for fueling start-up activity. As pointed out in Chapter 5, local resources in San Diego were created and reproduced as a consequence of participation and interactions. A large part of venture capital, angel investments and specialized services were created and utilized as a result of mutual engagements and communal initiatives, as shown in the San Diego Tech Coast Angels and the many partnership programs. In San Diego, many young entrepreneurs raised early-stage capital by being connected with seasoned entrepreneurs; many successful entrepreneurs invested their personal funding in biotechnology start-ups and provided advice to young entrepreneurs by participating in the San Diego Tech Coast Angels. Learning from this, policy makers ought to pay more attention to creating an environment where individuals have more interactions and engagement in communities. Urban amenities and geographic proximity can make a significant difference for local economic development by promoting interactions and involvement. In San Diego, UCSD and trade associations promoted interaction and communication between people: many entrepreneurs and scientists came out of the university and kept up interactions with colleagues by attending lectures and events at UCSD and CONNECT. The University Community Plan and its Scientific and Research Zone also played a pivotal role in generating the cluster by facilitating face-to-face interactions. Local governments might pay more attention to designing and developing a space that can unleash the creative power of social interactions.

Leadership and strategies are fundamental components in the development of the biotechnology industry in San Diego. During the 1980s, the public and private leadership shifted their focus from attracting large corporations from outside San Diego to nurturing small companies within San Diego. Collaborative initiatives from the late 1990s helped start-up companies address difficulties in recruiting talent and raising capital. More importantly, the community has developed a culture of collaboration in the process of setting agendas and leading efforts together. Interactions between biotechnology entrepreneurs and local governments resulted in more understanding and better relationships with their counterpart. A series of communal initiatives during the 1990s and 2000s contributed to enhancing local identity and understanding of their academic and industry counterparts. Participation and partnership do not only create better policies; they also produce a platform for interacting and collaborating. An angel investor, Jack Florio (interview), described how the experience of participation and engagements has changed the community: "I think that's part of what made San Diego as a great biotechnology community: the level of support that exists in this community, the level of collaboration, the ability to pull people from various companies around an issue to make something happen."

The research institutions in San Diego have created and adopted a set of rules and practices in the process of dealing with issues of technology transfer and interacting with their local biotechnology industry. Many academic scientists have developed the knowledge and practices to collaborate with industries through doing and interacting in their communities. UCSD is actively involved with local industries in many channels. In the last several years, the state government of Florida invested a large part of its funding in attracting campuses of TSRI and the Sanford-Burnham Institute to grow the biotechnology industry. The state of Florida wanted to bring in the knowledge and practices of these institutions related to technology transfer to nurture an industrial cluster, as well as their scientific capacity.

I suggest that programs and policies promoting technology transfer or the translation of academic research into economic activity focus on creating interactive environments where academics can easily engage with industries. Attention should be paid to encouraging academics to engage in communities of entrepreneurs and entrepreneurial activity. The accessibility and availability of advice from experts and colleagues about technology transfer help academics understand the process of commercial development. At the institutional level, UCSD, TSRI and the Sanford-Burnham Institute, which are important components of the regional economy, have developed rules and practices by trial-and-error through long-term involvement with industry. They have experienced conflict-of-interest and conflict-of-commitment by their members, but through effort and engagement, these institutions (more accurately their faculty and staff) have learned to leverage the power of industry to develop applications while maintaining academic integrity.

Technology transfer is also “a do-it-yourself process.” Individuals must experience interactions with industries to develop their knowledge and practices to collaborate with industries without breaching academic integrity, but to most individuals, it is a time-consuming and risky endeavor to engage in entrepreneurial activity. Universities and governments need to motivate and encourage academics to embark on development efforts if they want to facilitate technology transfer. Similar to the strategies to stimulate entrepreneurship, the focus must be given to individuals and their learning experience. A criticism by Dennis Carson (interview), director of UCSD Cancer Center, is informative to policy makers:

> You see a lot of Asian countries building giant biotechnology parks, but that's not gonna do it just putting buildings. They don't have the experience in the business, they don't have academic culture that promote independence by young people. There, professors control everything. So, there's very little reward for a young person to take risks and go out on their own.

In the end, policy makers ought to shift their focus from physical infrastructure to people, from large companies to small companies, and from individual companies to communities for learning and supporting in order to foster the development of clusters. To cultivate the interactions between research universities and industry, policy makers might consider giving more attention to encouraging academics to participate in the commercializing process and to engage with communities of entrepreneurs through grants and support, rather than seek to manage the technology transfer process. The magic takes place when individual academics learn how to participate in entrepreneurial activity and develop relationships with entrepreneurs. When connected and encouraged, many individuals might embark on their own ventures.

INTERVIEWS CONDUCTED (43)

| | |
|---|---|
| Greg Horowitt | Executive director of Global CONNECT (7/14/08) |
| Denise Lew | Senior licensing officer of Technology Transfer and Intellectual Property Services (TTO) at UCSD (1/26/09) |
| Julia Brown | Angel investor(member of the San Diego Tech Coast Angels)/ Formerly senior manager of biotech firms |
| Richard Atkinson | Formerly director of NSF (1975-1980), Chancellor of UCSD (1980-1995), President of the University of California (1995-2003) (2/26/2009) |
| Jonathan Chesnut | Director of Stem Cell Research and Regenerative Medicine at Life Technologies (formerly Invitrogen) (2/18/2009) |
| David Kabakoff | Executive in Residence of Sofinnova Venture, Formerly senior manager at Hybritech, Dura Pharmaceuticals and Salmedix (4/8/2009) |
| Mark Crowell | Vice president of Business Development at TSRI, Formerly president of Association of University Technology Managers (AUTM) (4/20/2009) |
| Jane Moores | Assistant Vice Chancellor of UCSD (Director of Technology Transfer and Intellectual Property Services) (4/20/2009) |
| Larry Bock | General partner of CW Ventures (6/9/2009) |
| Philip Low | Founder and CEO of NeuroVigil, Inc. (6/17/2009) |
| John Stuelpnagel | Founder of Illumina Inc. (7/9/2009) |
| Joseph Panetta | President and CEO of BIOCOM (10/2/2009) |
| Ralph Mayer | Chairman of Board of Governors of Tech Coast Angels (10/21/2009) |
| Raj Krishnan | Founder and CEO of Biological Dynamics (10/23/2009) |
| Michael Heller | Professor at the Departments of Nanoengineering and Bioengineering, UCSD (10/23/2009) |
| Rosibel Ochoa | Director of William J. von Liebig Center (10/26/2009) |

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|---|---|
| Tom Gable | CEO of Gable PR (11/25/2009) |
| Jack Florio | Vice President of Marketing & Communications at Tech Coast Angels (12/17/2009) |
| Russell Gibbon | Business Development Manager of the City of San Diego (12/17/2009) |
| Troy Wilson | President and CEO of *intellikine* Inc. (1/4/2010) |
| Kevin Kinsella | Managing director of Avalon Ventures (1/15/2010) |
| Kleanthis Xanthopoulos | President and CEO of Regulus Therapeutics Inc. (1/20/2010) |
| Paul Laikind | Chief business officer and Senior vice president of business development at Sanford-Burnham Institute for Medical Research (2/11/2010) |
| Ryan Bethencourt | Director of business development at California Clinical Trials (2/12/2010) |
| Jason Anderson | Vice president of business development at San Diego Economic Development Corporation (4/22/2010) |
| Jay Kunin | Vice president of BioMed Track at Tech Coast Angels (4/23/2010) |
| Wendy Johnson | President and CEO of Aires Pharmaceuticals Inc. (4/30/2010) |
| Peter Kuhn | Associate Professor of Cell Biology at TSRI (5/4/2010) |
| Dennis Carson | Director of Moores Cancer Center at UCSD (5/10/2010) |
| Rolf Muller | President and Chief Scientific Officer of Biomatrica Inc. (5/24/2010) |
| Scott Forrest | Director of Office of Technology Development at TSRI (5/28/2010) |
| Jacques Chirazi | Clean Tech Program Manager of the City of San Diego (05/28/2010) |
| Steven Flaim | President of Tech Coast Angels, Advisor at William J. von Liebig Center (6/1/2010) |

| | |
|---|---|
| William Fenical | Professor and director of Marine Research Division at UCSD (6/1/2010) |
| Eckard Weber | Partner of Domain Associates (6/30/2010) |
| Abigail Barrow | Director of the Massachusetts Technology Transfer Center, formerly managing director of William J. von Liebig Center (7/1/2010) |
| Gary Firestein | Director of UCSD Clinical Investigation Institute, Dean of Translational Medicine at UCSD (7/1/2010) |
| Daniel Pegg | Former president and CEO of San Diego Economic Development Corporation (1982-1997) (7/6/2010) |
| Michael Krupp | Advisor of William J. von Liebig Center (7/6/2010) |
| Mary Walshok | Associate Vice Chancellor for Public Programs at UCSD, Dean of University Extension and Adjunct Professor of Sociology (8/30/2010) |
| Irwin Jacobs | Director of Qualcomm, Founder of Linkabit and Qualcomm (9/22/2010) |
| Michael Rondelli | Director of Technology Transfer Office at San Diego State University (10/27/2010) |
| Duane Roth | CEO of CONNECT (since 2004) (11/24/2010) |

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