

# BIOTECHNOLOGY CLUSTER PROJECT

## SAN DIEGO ANALYSIS

Report prepared for the US Studies Centre by  
**Global Connect**

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# ABOUT

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# THE UNITED STATES STUDIES CENTRE PROGRAM ON INNOVATION

A KEY INITIATIVE OF THE UNITED STATES STUDIES CENTRE IS RESEARCH ON ISSUES OF HIGH IMPORTANCE TO BOTH AUSTRALIA AND THE UNITED STATES. THIS REPORT WAS SUPPORTED BY THE CENTRE'S RESEARCH PROGRAM ON INNOVATION, FUNDED BY THE MERCK FOUNDATION, WHOSE CONTRIBUTION IS GRATEFULLY ACKNOWLEDGED. THE PROGRAM'S OBJECTIVE IS TO ANALYSE THE ENVIRONMENT AND EXPERIENCE OF AMERICAN INNOVATION, IN ORDER TO DRAW CONCLUSIONS WHICH WILL CONTRIBUTE TO STIMULATING INNOVATION AND THE COMMERCIALISATION OF SCIENTIFIC AND TECHNOLOGICAL DISCOVERIES IN AUSTRALIA.

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**Biotechnology Cluster Project - San Diego Analysis**  
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## 1. Executive Summary

The United States Studies Centre commissioned Global CONNECT at UC San Diego to conduct an analysis of the development of San Diego's biotechnology sector over the past 35 years to provide insights that may be applicable to the Australian context. The research focuses on the important factors that contributed to the development of the cluster, while more deeply exploring several key issues identified in the first phase of the Australian portion of the project. These issues include understanding the context in which San Diego's research capabilities and biotech cluster emerged, the interaction with various levels of government, the role of early successes and flagship companies, the function and importance of intermediary organizations that support life science companies, and descriptions of two recent efforts by the San Diego community to pursue new multi-disciplinary opportunities in stem cell and algae biofuel technologies.

San Diego's current exceptional performance in the life sciences has its roots in a long history as a small business economy, driven by entrepreneurs, military contracting, and support for R&D. In their desire to retain the economic development benefits of military contracts after World War II, champions within the region took proactive steps through land use policies to build its R&D capacity, the most significant outcome of which was the founding of the UC San Diego campus in 1960. As important, many other research institutions were locating on the Torrey Pines Mesa just north of La Jolla at the same time, creating an "incubator without walls" for science and technology. The research institutions all adopted a strategy of recruiting world-class talent from the beginning to quickly establish themselves in the global scientific community, laying a solid foundation of intellectual capital for the biotech cluster that followed.

While the San Diego community experienced periodic economic ups and down, and was predominantly characterized by a local business culture, the research community continued to grow. Two critical events occurred that would begin the region's path towards developing leading technology clusters – the founding of Linkabit in 1968, the region's first wireless communications company, and the launch of Hybritech, the region's first biotech company, in 1978. Both companies were founded by UC San Diego professors: Irwin Jacobs in the case of Linkabit, and Ivor Royston for Hybritech. As these companies grew in parallel with the research community, the region became a magnet for new kinds of scientific, business, and finance talent to migrate to the region. It also stimulated the creation of new intermediary organizations such as CONNECT, which was focused on replicating the success of Hybritech and Qualcomm for broader-based, high value-added economic growth in the region. Our report highlights the impact Hybritech's success had on the growth of San Diego's biotech cluster.

From 1985 onward, there has been incredible momentum in the growth of San Diego's technology clusters, particularly in the life sciences. In this study, we document the critical

elements that contributed to San Diego's success through interviews and data analysis. A synthesis of the key findings which have emerged from the issues examined in this report are:

- San Diego is perceived to have fewer barriers to entrepreneurs than other regions.
- There is a long history of private-sector led initiatives, combined with a history of the State of California investing in infrastructure, that has built both the physical capacity (land available for development, UC San Diego, etc.) and a community that embraces more self-organizing principles rather than reliance on government-led programs for business development.
- The region's success in competitively securing large federal R&D grants is critical to the successful development of San Diego's high technology industries, particularly biotech.
- San Diego research institutions are highly interdisciplinary, entrepreneurial and competitive in their approach to pursuing R&D grants.
- San Diego's remoteness has been and continues to be overcome through strong personal links, proactive engagement with resources (talent, capital providers, strategic partners), and decision makers from outside the region, i.e. the Silicon Valley and Washington, DC.
- Flagship companies, such as Hybritech, helped launch San Diego's biotech industry in the 1980s. Going forward, consensus is emerging that a model of distributed partnerships among complementary firms within and outside of the region may reduce the likelihood of the region producing large, vertically integrated biotech firms.
- Diversity of the local economy and its assets is one of San Diego's strengths. Its diversity creates latent capabilities that can be leveraged when new technology opportunities arise, particularly in areas of convergence such as clean technologies or health IT.

Based upon these findings, we conclude with several questions about possible implications for the growth of biotechnology clusters in Australia. These include noting whether there is sufficient understanding of the social norm of collaboration, the presence of innovation intermediary organizations that facilitate the growth of social networks and provide support to biotech entrepreneurs, and whether the movement towards a more distributed model for biotech businesses creates an opportunity for Australian firms to overcome their geographic remoteness.



## Biotechnology Clustering Study – San Diego Analysis

### 2. Background

The United States Studies Centre at the University of Sydney has undertaken a comparative analysis of biotechnology clustering in Brisbane, Melbourne, Sydney, and San Diego. Work for this study was conducted in Australia during the Fall-Winter of 2009-2010. It included a survey of approximately 40 senior participants in Australia's biotechnology sector, followed by a landscape analysis which compared the regions on numerous quantitative metrics such as R&D expenditures, scientific publications, patent applications, and venture capital investments.

To complement this work, the United States Studies Centre commissioned Global CONNECT at UC San Diego to conduct an analysis of the development of San Diego's biotechnology sector over the past 35 years to provide insights that may be applicable to the Australian context. The research focuses on the important factors that contributed to the development of the cluster, while more deeply exploring several key issues identified in the first phase of the Australian portion of the project. These issues are:

#### *The Challenge of Remoteness*

San Diego, like regions in Australia, has had to overcome its remote location. San Diego continues to be shaped: (i) by public policies that are often established in other places such as Sacramento or Washington, DC; (ii) by the availability of resources, particularly capital from the Silicon Valley, as well as business management talent which was largely recruited from elsewhere; and (iii) by the need for strategic partners in the actual manufacturing and distribution of products. How does the biotech community deal with the challenge of remoteness in these three dimensions?

#### *The Role of Government*

How important have government policies been for the development of a biotech industry in San Diego? What should be the role of government in cluster development vis-à-vis public policy, public investment, and actual management of programs? What are the potential trade-offs of more or less involvement?

#### *The Role of Early Successes and Flagship Companies*

What has been the role of major successes and flagship companies in enabling the growth of the biotech cluster in San Diego? What impact do these events have on generating serial entrepreneurs, attracting people to the region, or retaining talent and companies in the region once they have located here?

#### *The Role of Innovation Intermediaries*

How effective are the connections today between various stakeholders and individuals in the San Diego cluster? What were the key elements in the development of these connections and

boundary-spanning activities, and what can be transferred to other regions? What are the effects of organizations such as CONNECT and BIOCOM, that facilitate and enable cross-sector linkages, as well as the creation of pre-transactional, trust-based relationships?

### *Seizing New Technology Directions*

To what extent is the San Diego region adapting its focus as new scientific problems and new technology opportunities emerge? How is its depth of expertise in biotechnology adapting to new market demands? What is the interaction between the evolution of ideas in scientific institutions and the impetus from the market place, as driven, for example, by the preferences of the venture capital community? Two recent cases, the emergence of collaborative activity in stem cell technology and algae-based biofuels, provide insight into this process.

These results and insights, presented here, are based on prior interviews with approximately two to three dozen individuals in the US and other countries on related topics, as well as 26 new interviews conducted specifically for this project with a cross-section of key individuals in the biotech cluster.

### **3. Interviews**

For this study, 26 individuals who could address various aspects of how San Diego's biotechnology industry developed were interviewed. A list of names and titles of interviewees is provided in the Appendix. Interviews were conducted either in-person or by telephone, averaged one hour, and were confidential. The interview questions were tailored to the individuals depending on their background and experience (i.e. government, academic, business executive, etc.), in order to draw out their unique perspectives on the topics the Australian team wished to have explored, such as the role of government or the challenge of remoteness.

A small subset of those interviewed were able to offer comparative perspectives on San Diego and Australia's biotechnology clusters, either due to their work experience and/or being Australian expatriates involved in the biotechnology industry in California. For this subset, a protocol of six questions similar to that utilized in the Australian survey was used in addition to more San Diego-centric questions. The full list of questions is provided in the Appendix as well as summarized responses of the respondents.

Based on the wealth of quantitative data on both Australia and San Diego provided in the Australian report, this study emphasized the qualitative dimensions of San Diego's biotech cluster. This study also offers additional quantitative performance data to complement the work of the Australian research team.

## 4. Context of San Diego's Biotech Cluster Development

### 4.1 The Challenge of Remoteness

Within the context of the continental United States, San Diego has been considered somewhat remote and isolated for most of its history. Located in the far southwestern corner of the country, bounded by the Pacific Ocean to the west, the Mexican border to the south, rugged mountains and desert to the east, and living in the shadow of Los Angeles to the north, it has frequently been referred to as the “cul de sac” of California. Transportation linkages with the outside world have been limited, reinforcing the region's remoteness. Rail connections to the East Coast have been on again, off again over the past century, and there has been a contentious, on-going fifty-year civic debate about building a true international airport with direct flights to other major cities. From a political perspective, San Diego is about as far from the state and national centers of power, Sacramento and Washington, DC respectively, as a city can be. Financially, it has been far from traditional banking centers in the east and, later, venture capital in the Silicon Valley. Citizens and local businesses have often struggled to cope with decisions made hundreds or thousands of miles away that impact their daily lives.

However, while still considered somewhat of a barrier, it could be argued that San Diego's isolation has fostered a unique set of collaborative community dynamics and was attractive to innovators and entrepreneurs, such that its growth as a robust knowledge economy has reduced its actual and perceived isolation significantly. Today San Diego is among the ten largest cities in the country, a major tourist destination, a scientific powerhouse, and is home to internationally recognized technology industries, such as wireless telecommunications and biotechnology. Global CONNECT's research and interviews have identified several factors that enabled the region to effectively overcome its remoteness. For instance, in part because of the absence of large, established industrial clusters, San Diego was a blank slate for scientific and biotech pioneers. The region offered these individuals the promise and freedom to build something from nothing. This was bolstered by the collaborative culture of the region, its readiness to integrate newcomers, and its ability to leverage the pre-existing relationships newcomers brought with them.

Unlike other leading regions in the country during the 1950s and early-1960s, San Diego lacked a reputation and infrastructure for scientific research. It also lacked large, well-established companies and institutions with bureaucratic traditions. While this lack of large successful enterprises could be perceived as a negative, or at least cause for hesitation by those considering a move to the region, the founders of the research institutions and biotech companies saw things differently. They viewed San Diego as an opportunity, a promising platform where one could start from scratch without having to be burdened by what had come before, either culturally or economically.

The notion of the region as a blank slate fed directly into San Diego's positioning as a place where people could pursue their scientific or business dreams. In order to build reputation and scientific impact immediately, the founders of the research institutions all set out to recruit world-class faculty from the beginning. To do that, they had to offer something other places could not, and that was the freedom to pursue the kind of research they wanted to do, in the manner of their choosing. One interviewee, who was recruited from Yale to establish UC San Diego's School of Medicine, noted that Yale had developed a culture of doing things that often constrained the work of faculty. UC San Diego promised no such constraints. The founding of the research institutions in the late-1950s and early-1960s was also happening at a time when the State of California was investing heavily in higher education, including research faculty and facilities. It also did not hurt that San Diego offered stunning weather in comparison to many East Coast cities. The combination of intellectual freedom, the opportunity to create new institutions from the ground up, access to greater financial resources, and beautiful weather nearly year round helped win over many of the scientists and researchers to the region despite its remoteness.

Later, founders of start-up biotech companies faced a similar challenge. They had to recruit management talent to a largely unknown industry in a region not known for high technology companies. Some candidates were concerned by the possibility of working for a start-up company in an emerging, high risk industry, in a place where there were very few alternatives should the company fail. However, like their academic counterparts who preceded them, those entrepreneurs who moved to San Diego were attracted by the opportunity to build something new in a cultural environment that lacked the constraints found elsewhere. The weather was also noted as a positive, and frequently used as a soft selling point to candidates from the East Coast.

Common to both the researchers and the entrepreneurs' experience was how these individuals leveraged their pre-existing personal and professional relationships. Although they were geographically remote, they were not sociologically isolated. All had ties to others outside of the region who possessed critical resources or access to support networks that were needed to be successful. These relationships were often formed in graduate school, post doctoral fellowships, or through prior business dealings. It was not uncommon to hear during interviews how once in San Diego, interviewees quickly activated their network of contacts in other cities to bring in additional business or scientific talent, capital, or business services. This openness to sharing resources and contacts is a key feature of San Diego's innovation ecosystem.

The opportunity offered by San Diego's blank slate attracted certain kinds of individuals with common traits. Because the region lacked a history of established institutions and families, it absorbed newcomers easily. Those who came to the region were bright, self-assured, relished the chance to do things differently, and in some measure possessed an irreverence for existing power structures. In several important instances, they developed this world view during their time at institutions that were beginning to embrace a more entrepreneurial culture, notably Stanford University and MIT. For example, Richard Atkinson, Chancellor of UC San Diego and later President of the University of California system, and Hybritech founder Ivor Royston both

had formative experiences at Stanford. Qualcomm founder Irwin Jacobs came to UC San Diego via MIT. These individuals and others like them translated their prior experiences to their work in San Diego, setting up new companies or creating new partnerships between research institutions and industry.

Changes in both telecommunications technology and the global economy have also reduced the challenge of remoteness. It is easier for scientific collaborators or business partners to interact via the phone or Internet today than it was thirty years ago. The nature of the biotechnology industry is also requiring many companies to partner across international boundaries, meaning that a company's geographic location is less important now than before. Interviewees noted that face-to-face contact is still required for many business dealings (hence a desire from the business community to have a true international airport), and a few felt that San Diego's geographic distance from venture capital in the Silicon Valley continues to put it at a disadvantage, particularly when capital is tight. However, the consensus is that remoteness can be overcome through a proactive strategy of collaboration and partnering. Several also stated that good ideas and solid business fundamentals will always get funded regardless of company location.

#### **4.2 Cultural Base for Collaboration**

San Diego's culture of collaboration and support for high technology entrepreneurs is the result of a multitude of factors that have influenced the region's development over the past 150 years. Its geographic remoteness from other parts of the country and lack of natural resources meant that residents had to continually take risks to find the "next big thing", sometimes resulting in success, other times resulting in failure. Further, like many West Coast cities built by pioneers, it has an open culture that welcomes newcomers and those with the ambition and skill to make a fresh start. Often these individuals would band together in economic development efforts, which included the dredging of the harbor to create a port, hosting the 1915 Panama-California Exposition, attracting and retaining a strong military presence, redeveloping the downtown urban core, and successfully advocating for new research institutions such as the Salk Institute, UC San Diego, and many others. It is in the latter efforts that San Diego has exhibited a strong culture of embracing and leveraging knowledge for social and economic benefit. This happened in 1903 when the Chamber of Commerce supported the founding of the Scripps Institution of Oceanography, continued through the 1950s, 60s, and 70s with the establishment of the major research centers, and is evidenced today in the bottom-up community support for intermediary organizations such as CONNECT and BIOCUM.

Because of the region's unique geographic and historical conditions, San Diego high tech entrepreneurs operate by a code of conduct that values participation. Those who do not collaborate with others, share of their time, or give back to the community may quickly develop a negative reputation. Collaborative behavior is continuously reinforced. To a certain extent, this behavior is enhanced and enabled by the tight concentration of companies and research institutions around the Torrey Pines Mesa. It does not require much time to meet with one's peers to exchange information or participate in events. Nor does it take much time for news, both good and bad, to spread throughout the community. In the end, the regional culture, as well as programs and activities put in place by support organizations, helps build the pre-transactional trust that is necessary for stakeholders to adapt quickly to the changing and uncertain conditions of knowledge-based industries.

### **William and Lillian Fishman and the La Jolla Cancer Institute**

The founding of the La Jolla Cancer Institute, which is today known as the Sanford-Burnham Institute for Medical Research, represents many of the characteristics that have made San Diego a hub for medical research and biotechnology companies. In the mid-1970s, William Fishman, at 65 years of age, faced mandatory retirement at Tufts University. However, he had just secured a \$250,000 NIH grant to continue his cancer research and wanted a place to work. He determined that he needed to find a place where he could continue to do his research in an environment that was intellectually dynamic but also an attractive place to live and work in his later years. He and his spouse Lillian landed in La Jolla in 1975 and were offered office space by the Salk Institute, the loan of an electron microscope by the UC San Diego Medical School, and immediately were supported by a women's auxiliary formed in La Jolla to help raise money for the development of their La Jolla Cancer Institute. They quickly attracted talented scientists to their Institute, secured major grants, and a large cash contribution from San Diegan Joan Kroc, of the McDonald's fortune, because she believed in their work. Over a brief period, this 1970s "startup" has evolved into one of the most distinguished centers of cancer research in the United States, with an annual research budget in excess of \$150 million.

## **5. Lessons from San Diego**

### **5.1 The Role of Government**

Interviewees with knowledge of both Australia and the US noted that on a general level, the US government is much less active than the Australian government in supporting industry. One could argue that the US does not have an industrial policy, although a long history of defense spending has shaped many sectors of the US economy. Rather, a mix of federal, state, and local government actions create a framework or environment that allows for institutions and companies to compete for resources. This is often done through incentives, tax policy, regulatory policy, patent policy, bankruptcy laws, research and education funding, and other

vehicles. San Diego's biotech industry has benefited from the interplay of government actions at the federal, state, and local levels that were often related, but initiated independently.

The US federal government impacts technology-driven industries in San Diego in three primary ways – through mission-oriented work typically performed under contract by private companies for the US military and other federal agencies,<sup>1</sup> the funding of basic research typically carried out by universities, and through regulatory processes, such as the phased clinical trials the US Food and Drug Administration (FDA) requires to demonstrate the safety of new drugs and medical devices.

One cannot understand the growth of San Diego's high technology industries without understanding the importance of defense-related spending and its development. San Diego's economy has long been tied to the US military through its naval bases, the defense contractor companies that later built up around the bases, as well as the military healthcare centers in the region. During and following the end of World War II, defense dollars supported the growth of a technically trained science and engineering workforce in the region. Keeping these high-wage jobs in San Diego was one of the key factors that led local advocates such as Roger Revelle from the Scripps Institution of Oceanography and John Jay Hopkins from General Atomics to push for the creation of a university as well as other R&D institutions during the 1950s. This resulted in the establishment of UC San Diego on the Torrey Pines Mesa just to the north of La Jolla, located on land partially occupied by two decommissioned military bases and adjacent to General Atomics and the Salk Institute. The region's wireless communications cluster, represented by companies such as Linkabit and later Qualcomm, both founded by Irwin Jacobs, grew out of serving the US military as a customer. The importance of the military continues to this day. A 2008 study estimated that approximately 8% of regional economic activity and nearly 24% of the region's employment is impacted directly and indirectly by US government defense spending.<sup>2</sup>

The most significant component of San Diego's biotechnology cluster is the federal government's R&D funding to research institutions across the Torrey Pines Mesa. Nearly every interviewee noted the importance of the increasing amount of R&D grants over the last twenty-five years to the growth of the cluster. As one interviewee stated, "The huge amount of federal funding to support research is critical. Without that, you don't get the research institutions, and without those, you don't get the cluster." What is important to note is that these grants are awarded on a competitive, peer-reviewed basis, meaning that only high-quality work gets funded. It also means that the region's researchers are themselves entrepreneurial in how they go after the money, with many large and interdisciplinary awards being won annually. Federal research funding fuels the development of new technologies, some of which may become commercialized by local biotech companies. Additionally, the funding supports a critical mass of scientific researchers in the region, many of whom may create their own companies, be hired

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<sup>1</sup> This is often referred to as R&D in the Department of Defense budget, but the work can be characterized more as development rather than research.

<sup>2</sup> San Diego Military Advisory Council, *San Diego Military Impact Study*, August 2008.

by local firms, or become scientific advisors to companies in the region. More detail on federal funding to the region is presented in Section 5.3 and in the Appendix.

The State of California has also played a role in creating an environment that supports the growth of the biotechnology cluster in San Diego. Firstly, for public universities, such as UC San Diego, the State provides funding that supports faculty, graduate students, and undergraduate students. This funding includes salaries, but also general support to the campus based on student enrollment. Secondly, the State provides funding for the facilities and infrastructure that supports research. The decision in the late-1950s to locate a UC campus in San Diego, and with that, the provision of funding to build world-class laboratories and other facilities, is an example. Thirdly, the State has periodically undertaken special initiatives that have enhanced San Diego's research capabilities.

Two State initiatives that have impacted San Diego are the creation of the California Institutes for Science and Innovation (Cal-ISI) at the beginning of the decade and the California Institute for Regenerative Medicine (CIRM) in 2005, which voters supported with a \$3 billion bond to be distributed over 10 years. Four Cal-ISIs were awarded on a competitive basis and each was required to meet a minimum two-to-one industry match for the State's \$100 million contribution. UC San Diego partnered with UC Irvine to create the California Institute for Telecommunications and Information Technology (Calit2). Together, they secured nearly \$300 million in industry matching funds. Calit2 is an interdisciplinary research center that builds collaborative teams of researchers and industry partners around projects that utilize advanced visualization and communications technologies. Several of these projects involve life sciences research, such as digitally enabled medicine or studying marine microbial genomics for potential medical applications. CIRM was established after the State's citizens voted for a bond to fund stem cell research in reaction to limitations placed on federal research grants during the Bush Administration. CIRM grants are also competitively awarded, and support both research and the construction of new facilities. CIRM's impact on San Diego is described in more detail in Section 5.6.1.

Local government's engagement with San Diego's research community has varied over time. During the 1940s and 1950s, it was heavily involved in making land use decisions regarding City-owned property on the Torrey Pines Mesa. The Mesa has become the "neighborhood" for 50 research institutions and the heart of the biotech cluster. The original intent was to support a growing demand for R&D by the military and military contractors. Large tracts of public lands on the Mesa were zoned for light industry, with the goal of attracting more research-oriented firms like General Atomics, founded in 1955. In 1959, the City of San Diego donated land for a new UC campus, as well as to Jonas Salk, discoverer of the polio vaccine, for the location of his research institute. Mayor Charles Dail was reported to be eager to provide Salk with a place on the Mesa, having suffered from polio himself.<sup>3</sup> While not anticipated at the time, the zoning

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<sup>3</sup> Nancy Scott Anderson, *An Improbable Venture: A History of the University of California, San Diego*, UC SAN DIEGO Press, 1993, pp 60-61.



decision was critical in making land available for the biotech firms that sprung up on the Mesa many years later.

Beyond land use decisions, local government has largely kept a hands-off approach to the local industry. However, during the late-1980s and early-1990s a severe drought had the City of San Diego considering water restrictions as a conservation measure. Led by David Hale, local biotech executives quickly organized themselves to educate the City Council on the importance of water to the industry, which is water-intensive. The concern was that restrictions could cripple the growing industry. The City responded by not imposing restrictions, but went further by creating an ombudsman position to interact with local companies, implementing business impact assessments for City decisions, and instituting a fast-track permitting process. The crisis over water use created awareness among the City government of the biotech industry and its needs. Since that time, relations with local government have been smooth, according to several interviewees. The current Mayor of San Diego, Jerry Sanders, has taken an active role in being visibly supportive of local technology industries, including biotech. He is a frequent speaker at industry events, supported the creation of a new trade association for clean technology companies, and has taken part in several San Diego delegation visits to Washington, DC to advocate on behalf of the community.

A vibrant innovation ecosystem depends on both a robust research capability as well as a robust entrepreneurial and business culture. The government can enable or cripple both. Most interviewees felt that government at multiple levels has been generally supportive. However, a few voiced concerns about the State of California. Over the years, they argued, the State has become increasingly unfriendly to businesses through increasing tax rates and regulations. There was also concern about its ongoing fiscal crises, which have resulted in large cuts to the state's education system, both at the K-12 level and for higher education, in recent years. These cuts may undermine the development of a technically trained workforce, the ability to retain highly productive research faculty, and the state's future ability to compete in high technology industries.

Another point to emerge from the interviews is the importance of having educated leadership. In order for the public sector to constructively support knowledge-based clusters, there is a need for technology-literate elected officials, and importantly, their staff. The importance of biotech executives meeting with City Council members is one example, but the region is also taking steps to increase awareness in Washington, DC through its delegation visits and the advocacy efforts of BIOCOM and CONNECT, two organizations created to support the growth of San Diego's life sciences and technology companies.

## **5.2 The Role of Early Successes and Flagship Companies**

Responses were interestingly mixed when interviewees were asked to name the major successes and/or flagship companies in San Diego's biotechnology cluster. On the one hand many cited the significant impact made by Hybritech, both for putting the region on the biotech industry map, but more importantly for bringing together a cadre of individuals who went on to become serial entrepreneurs who seeded the cluster with new, often successful companies.

On the other hand, some interviewees noted that San Diego has not produced biotech companies on the scale of Amgen or Genentech. Rather, it continuously produces small to medium-sized companies that are either acquired by larger firms from outside of the region, remain niche players, or fail. Both dynamics, a culture of serial entrepreneurship born out of the Hybritech experience and a “glass ceiling” for company growth, are in play within the region, and may point to a changing view on both the business model for biotech companies as well as San Diego’s role in a global industry.

During Hybritech’s heyday from the beginning of the 1980s to its acquisition by Eli Lilly in 1986, the company could clearly be described as a “flagship” firm for the region. At that time, there were few other successful biotech companies anywhere. Hybritech could be counted among a small group that included Genentech and Amgen. Its success is often attributed to the highly talented and effective staff, many of whom had been recruited from outside the region through pre-existing relationships. For instance, Ted Greene, the company’s first CEO, brought in several people he had known during his time at Baxter. Scientists who worked for the company often recruited former colleagues from previous positions at local research institutions. Given the start-up nature of the company, several employees who were scientists by training had to learn critical business skills such as product development or marketing, as there was no one else to fill these roles. While stressful, many stated in later interviews how much they enjoyed their time in such a creative environment.<sup>4</sup> Through Hybritech, they gained confidence in their abilities, and once the company was acquired by the more conservatively managed Eli Lilly which muted Hybritech’s exciting start-up culture, these individuals were ready to take the leap into forming new companies.

Several members of Hybritech’s management team went on to build new companies or become investors in new companies which contributed significantly to the growth of the cluster.<sup>5</sup> Among the most notable has been the success of Ted Greene and Tim Wollaeger. After Hybritech, they launched a small venture firm called Biovest. Biovest proceeded to finance six companies in an eighteen-month period, nearly all of which became successful. Several of these firms are still operating today and include Amylin, BioSite, and Vical, all of which benefited from Greene and Wollaeger’s guidance. Hybritech’s founder, Ivor Royston, also had his share of later success. His second company, Idec, grew to \$1 billion in annual revenues and later merged with Massachusetts-based Biogen to form what was at the time the world’s third largest biotech company. Like Greene and Wollaeger, Royston became an investor, setting up Forward Ventures, which in turn backed several new biotech companies in the region. Figure 1 shows the companies founded by Hybritech alumni from 1978 through 2002.

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<sup>4</sup> JD Ball and Richard J. Warburg, *Working to Improve Lives: The Secrets of the Biotech Industry from the Industry Leaders Featuring the San Diego Life Science Story*, National Institute of Science Media, 2006.

<sup>5</sup> Steven Casper, “How do technology clusters emerge and become sustainable? Social network formation and inter-firm mobility within the San Diego biotechnology cluster,” *Research Policy*, Vol. 36, pp 438-455, 2006. Mark Peter Jones, *Biotech’s Perfect Climate: The Hybritech Story*, Unpublished doctoral dissertation, University of California, San Diego, 2005.



research institutions, and is indicative of the region’s importance to the global life sciences industry.

**Table 1 Top 10 San Diego Biotech Companies by Employee Size**

Rank	Company	Local Employees	Revenues (\$s millions)
1	Illumina	1,635	\$573
2	Amylin Pharmaceuticals	1,500	\$840
3	Life Technologies	1,200	\$1,620
4	Genentech	480	N/A
5	Prometheus Laboratories	438	\$278
6	Santarus	345	\$130
7	Genoptix	329	\$116
8	Verenium Corporation	303	\$70
9	Isis Pharmaceuticals	299	\$107
10	Quidel Corporation	226	\$128

**Table 2 Top 10 San Diego Medical Device Companies by Employee Size**

Rank	Company	Local Employees	Revenues (\$s millions)
1	DJO Inc.	388	\$980
2	ResMed	255	N/A
3	Quidel Corporation	226	\$128
4	CardioDynamics International	125	\$24
5	Plastics Engineering & Development	105	\$12
6	Cytori Therapeutics	80	\$7
7	California MedTech LLC	69	\$21
8	SeaSpine, Inc.	42	\$41
9	ACI Medical	34	N/A
10	Ichor Medical Systems	21	N/A

Source: San Diego Business Journal, 2009 Book of Lists

This apparent cap or “glass ceiling” on company size is often attributed to San Diego’s reputation for starting new companies based on innovative technologies, and developing them to the point at which they become attractive acquisition targets by larger firms from outside the region. The acquirer will often pull the technology and/or the company to its headquarters location. Alternatively, in some cases, the technology fails in clinical trials, often resulting in a fatal blow to the company. Others increasingly become focused on filling particular niches, such as drug discovery or contract services. Combined, these three dynamics have created a cluster that is largely composed of small to medium-sized, innovative companies characterized by a high churn rate of firm failure and creation below the top tier. Nonetheless, these firms represent hundreds of millions of dollars in capital and thousands of jobs in the region. It is also the case that San Diego’s costly land prices, limited water supply, and high cost of living make it less suitable for large-scale manufacturing and distribution activities.

Our interviews revealed that there is less of a concern about the lack of large, flagship companies in the region than one might suspect. Several interviewees felt that both the nature

of the global biotechnology industry and San Diego's place within it are evolving due to a variety of factors. For many years now, because of the large capital costs required to successfully take a medical technology from the lab to market, most small biotech companies are forced to partner with larger firms that have the resources necessary to carry the technology through to the next stage of commercialization. This is most common among companies developing new drugs, which "copartner" with big pharma firms that are looking to fill their product pipeline. Simultaneously, globalization and the emergence of world-class capabilities in many countries allow biotech companies to outsource numerous functions that they previously developed internally at great expense (e.g. the fixed costs associated with building up staff, facilities, and equipment). These companies are under pressure from their investors and partners to do more with less to keep costs and burnrate down. The result has been an increasing trend towards small, "virtual" biotech companies that contract out or partner for services upstream and downstream on the value chain. This includes contracting for pre-clinical work, such as medicinal chemistry, screening, and animal testing – activities that were previously done in-house – to providers around the world.

Under a more "virtual", disaggregated model of drug development, companies must adopt a different management process. Executives must now juggle a wider range of relationships that are scattered around the world. They must also be adept at identifying who the appropriate partners are. This raises an interesting paradox – as the drug development business model becomes more globally distributed, it may increase the importance of regionally-based professional networks. Executives of small companies do not have the luxury of traveling around the world to find the right partners. Rather, they will often look to their colleagues and peers for referrals and insight on the quality of potential contractors or partners based on prior experience. In essence, they rely on their social network, many members of which may be found locally, for pre-qualified opportunities. Here, innovation intermediaries often play a valuable role by facilitating the development of social networks, and by providing a venue for vetting potential outsourcing partners. For instance, BIOCUM organizes delegation visits to China for its members to create new business partnerships. It also plans on signing an MOU in April 2010 with a Beijing development association to facilitate mutually beneficial opportunities.<sup>6</sup>

Duane Roth, CEO of CONNECT and an experienced biotech executive, has seen firsthand the inefficiencies of the old model of fully-integrated biotech companies for pursuing today's opportunities. Billions of dollars have increasingly been poured into drug development and yet the output of new FDA drug approvals is decreasing. Integrated firms with few products often implode after a failure in the clinic because they cannot continue to carry all the fixed costs associated with their infrastructure. Roth and co-author Pedro Cuatrecasas have proposed taking the virtual model of drug development to the next step.<sup>7</sup> Under their "distributed partnership model", firms focus on one or two of the four "Ds" in the process – Discovery

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<sup>6</sup> Heather Chambers, "Local Companies See Growth Opportunities in China", *San Diego Business Journal*, march 15-21, 2010, Vol. 31, No. 11, Pg. 1.

<sup>7</sup> Duane Roth and Pedro Cuatrecasas, *The Distributed Model for Drug Discovery and Development*, Ewing Marion Kauffman Foundation, January 2010.

Research, Definition Research, Development, and Delivery. Discovery of potential new drug candidates is done by research universities and institutions. Product definition companies (PDCs), comprised of small teams of experienced cross-functional managers, license multiple technologies that emerge from the discovery stage. The PDC then contracts with service providers to better define the potential of the technology and prep it for potential sale to venture capitalists, pharmaceutical companies, or larger biotech companies. The acquirers then work on the development stage to prepare the technology for market approval, either on their own or with service providers. This includes conducting advanced clinical trials, sorting out manufacturing issues, and working through the regulatory process. Once development is completed, the technology is moved into the delivery stage, which includes sales, marketing, and distribution, final manufacturing, and monitoring of the product. Because they already have the internal resources, sales networks, and manufacturing capabilities, delivery is handled by larger biotech companies and big pharmaceutical companies.

In the end, the distributed partnering model seeks to greatly improve the efficiency of the drug development process. According to Roth and Cuatrecasas, it shifts the emphasis from the growth of companies to the growth of more successful products. Firms move away from building fully integrated capabilities and instead focus on core competencies in one or two stages. This does not preclude the possibility that these firms will be successful and grow to be large players within their area of expertise. However, they will rely more on a number of service providers and partners than they do under the current model. San Diego's biotech cluster, with its high concentration of research institutions, small and innovative biotech companies, and lack of large-scale drug manufacturing capabilities, is positioned to fill the early stages of the distributed model. The cluster will continue to serve as a magnet for attracting talent and capital, but it also has the advantage of having already achieved a critical mass of capabilities over the past three decades. Roth and Cuatrecasas believe that the distributed partnership model does not require regions to have large concentrations of entrepreneurs and capital. Because the model is virtual, they feel that any region with high quality research will be able to attract attention from potential partners.

### **5.2.1 Growth of Specialized Business Support Services for Biotech Companies**

The success of San Diego's biotech cluster is due in part to the simultaneous growth of specialized business support services. Often overlooked in the discussion about how technology clusters develop, service providers such as law firms, real estate developers, public relations firms, accountancies and others play a critical role. Two examples of how service providers, specialized law firms and real estate developers, enabled the growth of the biotech industry in San Diego are illustrative.

Biotech companies rely heavily on protecting their intellectual property (IP). For many years, San Diego was "a legal backwater for IP" as one interviewee stated. Most firms were locally-based, dealt in more traditional areas of law, and served local clientele. Until the early 1980s, there were few, if any, law firms that offered specialized IP services to local technology companies. However, things began to change as the economy globalized and became more knowledge-based. Local lawyers were exposed to firms and professionals from outside the

region. In order to remain competitive against more sophisticated firms that operated at the national and international levels, they had to improve their capabilities by expanding their expertise and recruiting more talent. At the same time, the local client base began to change. There was growing demand for law firms that could represent technology clients. The local research institutions hired attorneys with a scientific background to assist with the technology transfer process, having being incentivized to do so under the Bayh-Dole Act. Later, as Hybritech and Qualcomm alumni and other entrepreneurs began founding companies, these law firms began doing more IP work for the business community. Outside firms, noting the increased activity in San Diego, opened offices to be closer to their clients. With the continued growth of the biotech cluster, the legal community developed a strong competency in specialized services. Today, with firms such as DLA Piper, Morrison & Foerster, Luce Forward, Fish & Richardson, Wilson Sonsini, and many others, San Diego's legal community is a leading source of legal services tailored for technology companies, including corporate law and IP protection. It has evolved from a legal backwater to one that attracts clients from many other regions in the US and around the world.

San Diego's technology companies also benefited from their relationship with local real estate developers. Co-founders of both Hybritech and Qualcomm have noted that developers worked with their companies in their early days to get into office space they could not otherwise afford, either through reduced rent or structuring the deal in a way that lowered up-front costs. "Venture real estate", as it is termed when developers share risks with the technology startup companies, took root in San Diego and was a key component in the growth of the biotech industry.

In the early-1980s, there were few spec-built office buildings equipped with laboratory space for local biotech companies. The only option was to convert existing office buildings that had not originally been set up to handle labs. Accommodating the needs of biotech companies, either building lab space from the ground up or by converting an existing building, is an expensive proposition. This is an obvious challenge for cash-strapped biotech companies with limited resources. Mike Ready at Nexus Development was among the first to offer a solution, beginning with a couple of projects on the Torrey Pines Mesa. Rather than have the tenant pay the building improvement costs at the beginning, Ready amortized the costs into the rent, allowing them to be covered more easily by biotech startups with limited cash. Other developers, such as Burnham Real Estate (now part of Cushman & Wakefield), took notice and quickly followed suit. By the mid-1980s, biotech had emerged from its uncertain beginnings and had become a rapidly expanding industry. There were already some stunning successes with Genentech, Amgen, and Hybritech, and few failures at that point. From the perspective of the developer, taking on the costs of constructing buildings with expensive wet labs was a worthwhile bet. They got a return on the improvements because they were able to charge premium rents, and they felt there was sufficient demand that they could quickly get a new tenant should the current one go under. The situation today is more difficult now that the risks associated with the biotech business are better known. Developers can still work with client companies and lenders, but it requires the biotech company to have more cash on hand and offer greater guarantees.

As with biotech entrepreneurs, San Diego attorneys and real estate developers successfully leveraged their social networks. They relied on referrals from professional contacts, grew their network via participation in organizations like CONNECT and BIOCOM, and worked other networks as well, such as connections made within the scientific community during earlier phases of their careers. Many service providers offered pro bono or discounted services to capital-constrained start-up companies, which is a form of shared risk. They also actively integrated the local social norms that support efforts to volunteer time, share contacts, and give back to the community, primarily through intermediary organizations such as CONNECT and BIOCOM.

### **5.3 Funding of life sciences research in San Diego**

As noted earlier, research is core to San Diego's life sciences cluster. Federal R&D funding to San Diego was approximately \$1.2 billion in FY 2009, up from \$889 million in FY 2008. This is based on data from the National Institutes of Health (NIH), the National Science Foundation (NSF), NASA, and the National Oceanic and Atmospheric Administration (NOAA). Department of Defense (DOD) and Department of Energy (DOE) data on regional funding are not included due to difficulties clarifying what proportion of their funding is for R&D and data availability (although many estimate this to represent significant additional funding annually).<sup>8</sup> NIH is the largest source of R&D grants to the region. In FY 2009 NIH awarded San Diego \$919 million, or nearly 77% of the total, across 2,244 awards. In comparison, FY 2009 funding from the National Science Foundation (NSF) was \$267 million. NASA and NOAA funding combined totaled \$30 million. Due to the defined missions of the federal agencies, it is assumed that nearly all NIH funding is used to support biological and medical sciences research. While the other agencies may support work in these fields, it is likely a very small proportion. It is important to note that FY 2009 funding totals include grants awarded under the American Recovery and Reinvestment Act of 2009 (ARRA), the economic stimulus package. ARRA provided a significant boost nationally to both NIH and NSF research budgets. These increases are not expected to be maintained once the two-year ARRA funding period ends in FY 2011.

Table 3 shows the top seven NIH grant-receiving institutions in San Diego for FY 2009 by award amount and number of awards. ARRA funding, which is included in the totals, is also listed to indicate the size of increased funding the region was competitively awarded via the stimulus package. The amounts represent the total funding for the life of the grant awarded in FY2009, many of which are for multiple years. UC San Diego's cornerstone role in the region's life sciences research enterprise is clear, having captured 46% of the total NIH funding and 45% of the total number of awards. For all recipients, the average grant size was \$325,000, with a median duration of five years.

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<sup>8</sup> DOD funding often comes in the form of contracts to support technology development, as well as grants. DOD reports often combine R&D with testing and evaluation activities.



**Table 3 Top 7 NIH Grant Recipients FY 2009**

Institution	Total NIH Award Amount	Total # of NIH Awards	NIH ARRA Amount	NIH ARRA Awards
UC San Diego	\$421,904,076	1,018	\$50,484,818	183
The Scripps Research Institute	\$257,167,720	519	\$43,602,452	116
Sanford-Burnham Institute	\$77,725,139	126	\$11,351,181	31
Salk Institute	\$45,842,331	104	\$6,652,817	17
La Jolla Institute	\$36,752,133	53	\$2,649,335	9
San Diego State University	\$35,357,299	114	\$7,795,075	34
Veterans Medical Research	\$15,652,600	43	\$3,121,023	9
<b>Total</b>	<b>\$890,401,298</b>	<b>1,977</b>	<b>\$125,656,701</b>	<b>399</b>

Source: National Institutes of Health

### 5.3.1 Funding at UC San Diego

For FY 2009 UC San Diego reported total research contract and grant obligations of \$881.6 million.<sup>9</sup> Obligation amounts represent those dollars authorized to be spent on projects during that year, rather than for the full life of the grant. Table 4 shows a breakdown of research funding by School/Division.

<sup>9</sup> UC San Diego Office of Contract and Grant Administration, 2009 Annual Report. Detailed tables are available at [http://ocga.ucsd.edu/OCGA/Annual\\_Reports/2009/Overview.htm](http://ocga.ucsd.edu/OCGA/Annual_Reports/2009/Overview.htm).

**Table 4 UC San Diego Research Contract and Grant Obligations, FY 2009**

Campus Area	Obligation Amount	% of Total
<b>General Campus</b>		
Interdisciplinary Organized Research Units (ORUs)	\$88,426,113	10.0%
Jacobs School of Engineering	\$67,087,277	7.6%
Division of Physical Sciences	\$42,819,440	4.9%
Division of Biological Sciences	\$33,737,063	3.8%
Other General Campus Units	\$16,768,875	1.9%
Division of Social Sciences	\$11,215,888	1.3%
International Relations & Pacific Studies	\$791,381	0.1%
Arts & Humanities	\$68,902	0.0%
<b>Health Sciences</b>		
Departments & Schools	\$431,954,015	49.0%
Interdisciplinary ORUs/Other	\$62,325,225	7.1%
<b>Scripps Institution of Oceanography</b>	\$126,430,418	14.3%
<b>Total</b>	<b>\$881,624,597</b>	<b>100%</b>

Source: UC San Diego Office of Contract and Grant Administration

Additional detail on funding to UC San Diego and how resources are allocated are provided in the Appendix.

#### **5.4 The Role of Innovation Intermediaries**

The success of San Diego’s high technology industries has often been attributed to the catalytic role of organizations such as CONNECT and BIOCUM in the commercialization process, due to their ability to bring disparate stakeholders together to support the growth of new, innovative companies.<sup>10</sup> These “intermediary” organizations span multiple boundaries in the community by actively engaging entrepreneurs, research institutions, investors, attorneys, real estate developers, marketing specialists, and government representatives, among others.

Intermediary organizations convene meetings, organize events and research briefings, and enable a variety of activities that assure the knowledge flows, the development of pre-transactional relationships, and the trust building essential to working on highly uncertain, risky ventures. Further, activities and frequent interactions among diverse stakeholders create a community based on a culture of collaboration, a shared vision for the future, and a willingness to share risk, instilling a spirit of “community over company”.

<sup>10</sup> Michael Porter, *Clusters of Innovation Initiative: San Diego*, US Council on Competitiveness, May 2001.

The presence of CONNECT and later BIOCUM was critical during the formative period of the region's high technology clusters in the 1980s and early 1990s, because the region lacked a critical mass of entrepreneurial talent and business support services. If the region was going to build successful companies, local leaders recognized that they had to increase the quality and quantity of business know-how in the region and collaborate in order to compete with those in the Silicon Valley, Boston, or elsewhere.

CONNECT was created in 1985 in response to the region's lost bid to Austin, Texas for the Microelectronics and Computer Technology Corporation's (MCC) headquarters. MCC was a consortium of leading American semiconductor and computer manufacturers. A small group of regional business leaders worked with then UC San Diego Chancellor Richard Atkinson to develop a program they believed would accelerate innovation and entrepreneurship in the region. This was a wholly bottom-up, privately funded initiative, endorsed and administratively supported by UC San Diego. The founders chose to base the program within the university to ensure that it was viewed as a neutral broker in the community, rather than perceived as having a bias towards a particular industry or institution.

Numerous interviewees indicated the significant impact CONNECT's first CEO, Bill Otterson, had on the community. It was critically important that the CONNECT founders identified a uniquely qualified person to lead this effort. Approximately six months after the establishment of CONNECT the founders hired Otterson, an irreverent and successful entrepreneur with extraordinary connections and boundless energy. As a consequence, Otterson was able to integrate the disparate communities essential to a successful innovation system.

Through its early activities and programs, CONNECT members shared their business contacts and professional networks to benefit others. Networking events and lecture series, such as Meet the Researcher and Meet the Entrepreneur provided a venue for stakeholders from different parts of the community to get to know one another and the work they were involved in. Early on, CONNECT's Biotechnology Corporate Partnership Forums became important events for attracting interest in San Diego's emerging biotech industry from outside the region. In later years, the Springboard Program began a process of coaching and mentoring entrepreneurs that continues to this day.

In 2005, after 20 years of being anchored in the university, CONNECT spun out an independent non-profit to better represent the broader region. Duane Roth, who comes from a background in the pharmaceutical and biotech industry, became CONNECT's third CEO that same year. Roth has proceeded to reinvigorate the organization's membership base, while also better integrating the large number of research institutions that now exist on the Torrey Pines Mesa. The organization now has a \$3 million annual budget and 17 staff members. It holds over 330 events each year that attract approximately 15,000 attendees. As it did with BIOCUM's predecessor, the Biotech Industry Council (BIC), CONNECT continues to support the development of new trade associations, including CleanTECH San Diego and Sports Innovators in the past two years. It also manages and provides administrative support to other organizations, such as the Tech Coast Angels and the MIT Enterprise Forum. In February 2010,

CONNECT launched a \$400,000 effort to open an office in Washington, DC to advocate on behalf of the region's innovation economy.

BIOCOM, a life sciences industry trade association, is the other significant innovation intermediary for San Diego's biotechnology cluster. It was founded in 1995 from the merger of two pre-existing organizations, the Biotech Industry Council (BIC), which was made up of industry executives, and the Association of Biotechnology Companies (ABC), which was comprised of representatives from the service provider community (public relations firms, real estate developers and architects, lawyers, etc.). Led by David Hale, a former Hybritech CEO and co-founder of CONNECT, the BIC was established in response to the need for educating local government about the industry and to advocate on behalf of its member companies. At that time, CONNECT was restricted from undertaking advocacy because of its affiliation with a public university. Bill Otterson was a strong supporter of creating a new organization. He understood the need for the biotech community to have its own voice now that there were several successful companies in the region. For a time after the merger, the organization was given space at Mycogen, a local ag-biotech firm, and it began holding industry-specific events and launching initiatives such as a purchasing group and investor forums. Joe Panetta, who had been Mycogen's Vice President for Government and Public Affairs, took over the role of President and CEO of BIOCOM in 1999 and continues to lead the organization today.

Today, BIOCOM has grown into the largest regional life sciences trade association in the US with a staff of 17, an annual budget of approximately \$4 million, more than 550 members, and hosts more than 80 events a year ranging from networking receptions, to investor forums, to its Annual Gala, all of which attracts approximately 6,000 attendees. Advocacy on behalf of its members at the state and federal levels is one of its core functions. The organization has also created several specialized programs to benefit its members. One of the earliest and most important is the BIOCOM purchasing group, which helps members generate savings from vendors through higher-volume purchases and more favorable terms for products and services. BIOCOM has also been very active in supporting workforce development initiatives. It has worked with the San Diego Workforce Partnership, a non-profit organization that serves as a regional office for coordinating job training efforts and delivering assistance to the unemployed and underemployed, as well as local education providers to develop new curriculum at the K-12 and college levels in life-science related fields. Its most recent initiative involves a three-year, \$4.95 million job training grant from the US Department of Labor awarded in February 2010. Called the Biotechnology Readiness, Immersion, Certification and Degrees for Gainful Employment (BRIDGE), BIOCOM has partnered with the San Diego Workforce Partnership, San Diego State University, and the Southern California Biotechnology Center at Miramar College (a community college) to offer education, training, and job placement services in the region's life sciences industry.<sup>11</sup>

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<sup>11</sup> San Diego Daily Transcript, "Regional project for more biotech jobs receives grant", February 17, 2010.

## 5.5 Financing of San Diego Life Science Companies

Benefitting from the richly funded basic research activities in the region and the talent they represent, San Diego is a promising environment for technology commercialization and biotech industry development. However, this requires access to different forms of capital and know-how than one finds in the basic research environment. San Diego biotech companies draw on a range of distinct sources for capital as they move through each stage of development and growth.

### 5.5.1 Angel Capital Investments

Angel investors provide very early-stage capital for San Diego technology products and companies. While many angels operate independently, organized groups have formed over the years, allowing members to share collective intelligence about opportunities, team together for deals, and share due diligence tasks. There are now approximately 300 organized angel groups in the US and Canada.<sup>12</sup> San Diego angel groups include the Life Science Angels and the San Diego chapters of the Tech Coast Angels (TCA) and Keiretsu Forum. TCA is the largest angel investor group in the US, with over 250 members based in its five chapters, all located in Southern California. The San Diego chapter has approximately 70 members who meet regularly each month and are provided administrative support by CONNECT.

Unlike most angel groups, many TCA deals are captured by the Thompson Reuters VentureXpert database. Using this source, across all five chapters, there were 79 deals valued at nearly \$70 million from 1999 to 2009. Only seven were in biotech, six of which were in San Diego. Two of the four deals in the medical/health sector were in San Diego-based companies. Because of the large amounts of capital that most life science companies require to get their products to market, angels tend to invest in other types of technologies, such as software or IT. When they do invest in life science companies, it is rare that they back drug discovery and development firms, preferring less capital-intensive technologies such as diagnostics or medical devices. That said, three of the six biotech companies TCA supported in San Diego between 2001 and 2008 involved some form of therapeutic or delivery platform technology. There were no life science deals reported by the San Diego TCA chapter in 2009.

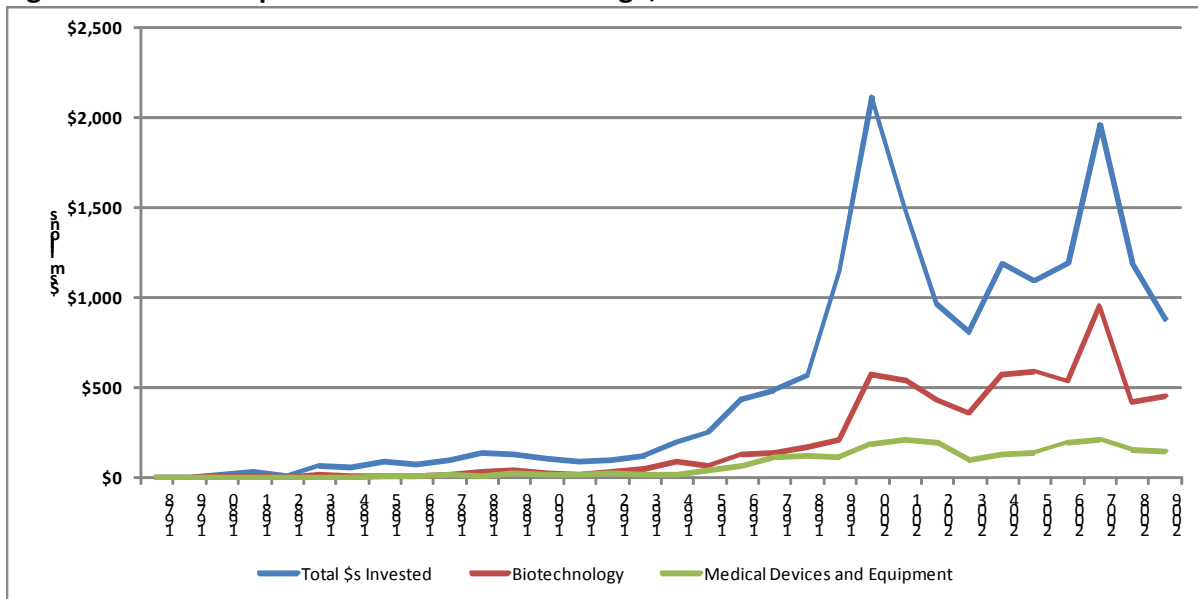
### 5.5.2 Venture Capital Investments

Part of the success story for San Diego technology clusters is the growth of venture capital investments since the late-1970s, when such deals were nearly non-existent. Today, San Diego is only superseded by the Silicon Valley and Boston, and runs neck-and-neck with the Los Angeles/Orange County region in terms of the total dollars invested annually in promising companies. Figure 2 shows the amount of venture capital invested in the San Diego region overall, as well as into the biotech and medical device sectors, from 1978 (the year Hybritech was founded) to 2009. In 2009, of the \$884 million invested, biotech companies received \$457 million, or 52%, of the total, while medical device companies raised nearly \$150 million in financing, or 17%.

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<sup>12</sup> Angel Capital Association, *ACA Member Landscape – 2009*. Available at <http://www.angelcapitalassociation.org/data/Documents/Press%20Center/ACA%20Statistics%202009.pdf>.

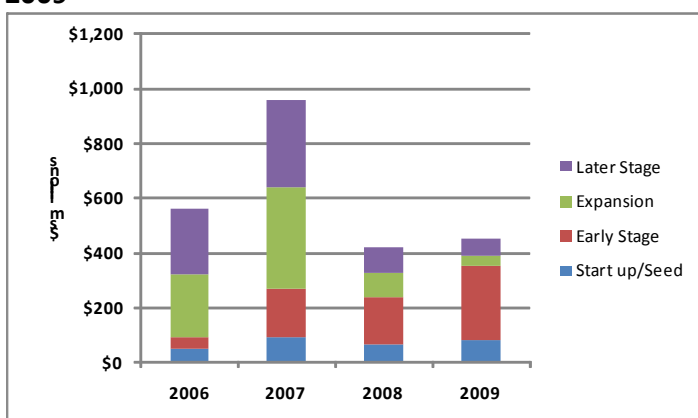
**Figure 2 Venture Capital Investments in San Diego, 1978 - 2009**



Source: Thomson Reuters VentureXpert

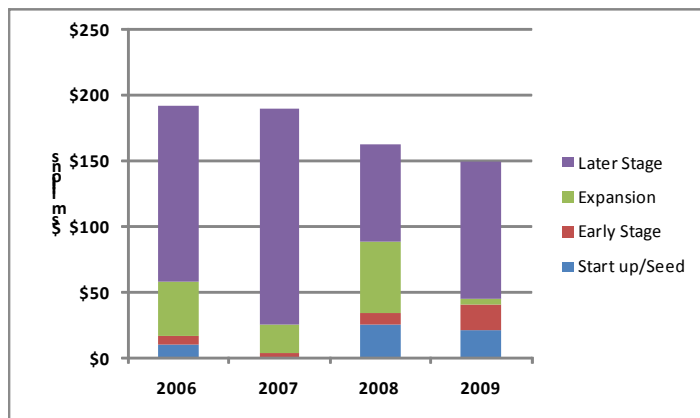
Early stage investments in biotechnology companies increased during the past four years, totaling \$272 million in 2009, or 60% of all investments going into biotechnology firms. As can be seen in Figure 3, investments in the expansion and later stages declined dramatically. This may be due to companies finding alternative means of securing resources, such as mergers and acquisitions. Alternatively, it may also be due to a smaller number of companies reaching that stage of development. Figure 4 shows that for medical device deals, later stage investments dominated all four years.

**Figure 3 Venture Capital Investments in San Diego Biotechnology Companies by Stage, 2006 - 2009**



Source: Thomson Reuters VentureXpert

**Figure 4 Venture Capital Investments in San Diego Medical Device Companies by Stage, 2006 – 2009**



Source: Thomson Reuters VentureXpert

Most venture financing comes from investors with headquarters located outside of San Diego. Silicon Valley firms are the most common, but investors also hail from Chicago, Boston, New York, and as far away as London, Madrid, and Taipei. Several firms have set up satellite offices within the region to better prospect for deals. These include firms such as Sanderling Ventures and ProQuest Ventures, among others. In 2009, a handful of locally headquartered VC firms financed life sciences companies in the region. Five of these (Hamilton Bioventures, Biogen Idec Ventures, Enterprise Partners, Forward Ventures, and Mesa Verde Venture Partners) participated in 12 local deals. This is out of 69 total deals involving 51 biotech and medical device companies. It is difficult to determine the amount of money invested by local firms given that VentureXpert only reports the total amount invested by the syndicated partners.

Overall, most venture capital financing for life science companies comes from managed funds. In 2009, six corporate funds participated in seven deals. The investors were Dow Chemical, Novartis Venture Fund, Biogen Idec Ventures, Lilly Ventures, Genzyme Ventures, and Kaiser Permanente Ventures. Three of the deals took place at the seed stage, two in the early stage, and one each in the expansion and later stages. Corporate venturing in 2008 was somewhat different. Eight funds invested in 11 deals, seven of which were in the expansion stage. There were zero deals in the seed stage, one early stage, and three later stage deals that year.

### 5.5.3 Mergers and Acquisitions

Mergers and acquisitions (M&A) are another means by which San Diego life science companies can get access to new resources (via their acquirer). Because stock market conditions during the past couple of years have been unfriendly to initial public offerings (IPOs) by technology companies, M&As offer one of the few opportunities for early investors to cash out or exit. Table 5 shows M&A activity in California during 2009. According to data collected by CONNECT and its partners, activity in San Diego represented 14% of the deals and 11% of the total reported transaction value within the state. There was a notable increase in the value in Q4 2009, which included the \$402.5 million acquisition of Calixa Therapeutics by Lexington, Massachusetts-based Cubist Pharmaceuticals, and the \$77 million deal for BioDuro, LLC by

Pharmaceutical Product Development, Inc., which is headquartered in Wilmington, North Carolina. These two deals represented 38% of the total M&A transaction value for San Diego in Q4.<sup>13</sup>

**Table 5 M&A Activity in California, Q1 – Q4 2009**

Region		2009 Q1	2009 Q2	2009 Q3	2009 Q4	2009 Totals
Northern CA	Total Report Value (in Millions)	\$4,949	\$1,866	\$2,520	\$17,134	\$26,469
	# of Closed Deals	91	89	155	136	471
Southern CA	Total Report Value (in Millions)	\$6,195	\$1,169	\$1,1827	\$3,181	\$12,372
	# of Closed Deals	103	74	134	131	442
San Diego	<b>Total Report Value (in Millions)</b>	<b>\$2,703</b>	<b>\$139</b>	<b>\$99</b>	<b>\$1,250</b>	<b>\$4,191</b>
	<b># of Closed Deals</b>	<b>42</b>	<b>24</b>	<b>32</b>	<b>29</b>	<b>127</b>

Source: IQ Capital; Roth Capital Partners; CONNECT

#### 5.5.4 Private Placement Investments to Public Companies

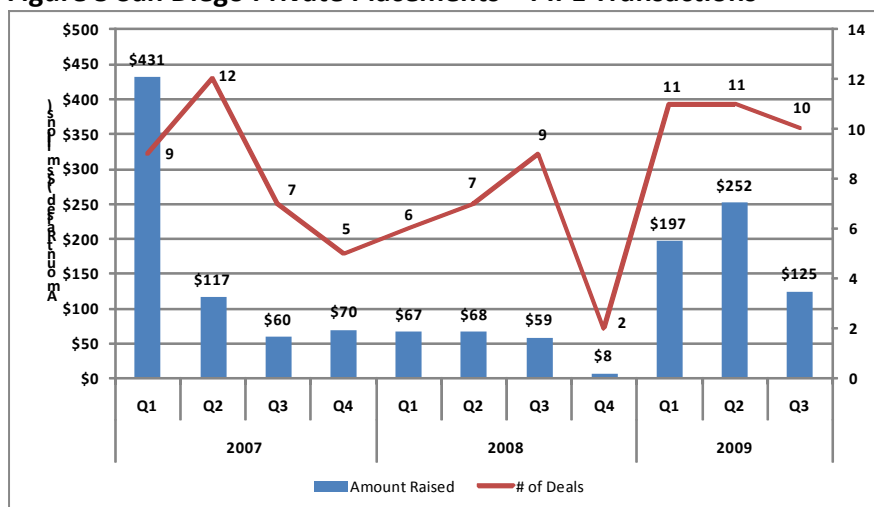
Private Investment in Public Equities (PIPE) transactions are another means by which public companies, often small to medium-sized firms, can raise capital. According to Sagient Research, PIPE transactions are defined as privately negotiated sales of companies' securities to individual accredited investors or institutional funds. Such transactions are attractive because they typically are a faster and cheaper means of getting capital versus a public offering, particularly when public markets have been effectively closed to new offerings. Figure 5 shows the total amount raised and number of deal via PIPE transactions involving San Diego companies from Q1 2007 through Q3 2009, the latest quarter for which information is available. The impact of the economic recession, which limited the value of the deals, is readily apparent in the figures for most of 2007 and all of 2008. In Q3 2009, PIPE transactions in San Diego were dominated by life science firms, with 5 deals totaling \$56 million. Of this amount \$44 million was raised by biotech companies, \$6 million in the pharmaceutical sector, and \$3 million in medical devices.<sup>14</sup>

<sup>13</sup> CONNECT Innovation Report, Third Quarter 2009

<sup>14</sup> Ibid.



**Figure 5 San Diego Private Placements – PIPE Transactions**



Source: Sagient Research Systems (PlacementTracker); Roth Capital Partners; CONNECT

This activity raises a question about how companies find potential investors and vice versa. Specialized investors tend to keep track of cutting-edge developments in their field, through referrals within their network, reading industry publications, and attending industry or scientific conferences. In this manner, they will come across firms that are pushing new technology boundaries and may be good investment opportunities. Companies get knowledge about potential partners and investors from the members of their global business and scientific advisory boards, as well as from active use of their social networks and innovation intermediary organizations. San Diego’s highly integrated boundary-spanning innovation community enables easy and rich forms of information-sharing about opportunities and sources of capital. Both CONNECT and BIOCUM regularly offer forums that place companies in front of potential investors.

### 5.6 Seizing New Technology Directions

San Diego’s research and high technology business community readily adapts to new opportunities. The diversity of research activities going on in the region and the robust innovative business community represent a “readiness” to pursue new entrepreneurial directions. The early growth of the biotechnology and wireless communications clusters is an example of this adaptability. Today, the community is adapting to areas of convergence between two or more pre-existing technology sectors, such as clean technology and wireless health technologies. Two examples of how members of the community are coalescing around new opportunities, stem cells and algae biofuels, provide insight into how this happens.

These examples share several common characteristics. In both cases, local academic researchers were conducting research on the topic in relative obscurity. When market conditions changed and additional resources became available, either through increased government funding or potential business opportunities, these scientists were in multiple, pre-existing relationships with colleagues in neighboring research institutions and with champions

from the local business community. This enabled the rapid development of more formalized partnerships to collectively pursue expanding public and private resources. Innovation intermediary organizations, such as CONNECT, BIOCOM, and CleanTECH San Diego play a critical role in facilitating these partnerships through networking events and public forums, which share knowledge about who is doing what in science and technology in the region, and quickly facilitate opportunities to grow new capabilities and technology sectors.

### **5.6.1 San Diego: A Hub for Stem Cell Innovation**

In a few short years, the San Diego region has become a hub for cutting-edge stem cell science. This is due in large part to leaders in the research and business community rapidly coming together to develop innovative and collaborative partnerships that leverage complementary strengths and pre-existing professional relationships. This activity has come about as a bottom-up reaction to events taking place at the national and state levels, and provides a critical context to understanding why San Diego has been so nimble in adapting to this promising new opportunity.

The first human Embryonic Stem Cell (hESC) was isolated in 1999 at the University of Wisconsin by Dr. James A. Thomson. This achievement catalyzed research around the world on a biological tool that has the ability to differentiate into any type of human cell, and offers hope for the cure of any number of human ailments. However, the discovery also raised ethical concerns that led to the US government placing limitations on the types of stem cell research it would fund. Restrictions on the use of human embryos in federally-funded research had been in place since 1995, but became tighter at the end of 2001. Newly elected President George W. Bush announced that federal funding would only be available for research on stem cell lines already in existence.

In 2004, after receiving pressure from research institutions and scientists who feared losing the opportunity to work on a promising area of science, Congress began to take action. Over the next year, the House and the Senate tried to pass five separate pieces of legislation to loosen stem cell restrictions. One of these, the Stem Cell Research Enhancement Act passed Congress but ultimately had no effect. Indicating his strong moral objections to this area of research, Bush exercised the first legislative veto of his presidency. The veto effectively stalled progress on stem cell funding at the federal level until President Obama announced revised guidelines in 2009.

After the first Bush veto, states took independent action to develop funding opportunities for stem cell research—first New Jersey and later California. In California, there is a process whereby voters can put an initiative or ‘proposition’ on the ballot during an election to create a new law or amend the constitution of the state. In 2004, Proposition 71 was developed with the goal of establishing a California Institute for Regenerative Medicine (CIRM), which would authorize the state legislature to issue \$3 billion in grants, funded by bonds, over ten years for research in stem cells and other related biomedical fields. The Institute put in place an Independent Citizens’ Oversight Committee (ICOC) to ensure its accountability to voters.

The campaign for Yes on Proposition 71 spent over \$30 million, money received from entrepreneurs, celebrities, and venture capitalists. Led by Robert Klein, a real estate developer who authored the initiative and was its principle financier, Proposition 71 was also supported by eBay founder Peirre Omidyar, Microsoft's Bill Gates, and John Doerr, a partner at the prominent venture capital firm Kleiner Perkins. Klein's avid support of stem cell research is attributed by many to the fact that his son has diabetes and his hope that stem cell research can find a cure.

After Proposition 71 passed with 59% of the vote, a remarkable accomplishment given the narrow scientific focus of the measure, the California Bioethics Council and other taxpayer groups filed numerous lawsuits with the California Supreme Court contesting the constitutionality of the measure, which delayed the distribution of funding. In the meantime, venture capitalists loaned the state \$14 million to start approving grants, and in 2005 Governor Schwarzenegger granted a \$150 million loan to help the group continue operations until the cases in court were resolved. In February 2007, with a 3-0 ruling, the First District Court of Appeal in San Francisco denied claims by opponents of embryonic stem cell research and allowed CIRM to finally distribute funding.

Shortly after voters approved Proposition 71, CIRM began a search for the city in which to build its headquarters via a competitive bid. Seeing an opportunity to enhance San Diego's position as a leader in the life sciences, the regional community of research institutions and businesses quickly assembled a strong proposal for the headquarters to be located on the Torrey Pines Mesa among the cluster of research institutions and biotech companies. This effort was led by individuals such as Julie Meier Wright from the San Diego Regional Economic Development Council, Duane Roth of CONNECT, and Larry Goldstein, a prominent medical researcher at UC San Diego. As part of the bid, multiple partners pledged millions of dollars worth of office space and housing. Qualcomm founder Irwin Jacobs even provided use of his private plane for the San Diego delegation to travel to Fresno to hear the final decision.

Although San Diego came in second to San Francisco for CIRM's headquarters, the experience created new relationships and reinforced a collaborative spirit among those who participated. In 2005, having already hired a number of researchers (in part, thanks to local, privately funded new endowed chairs) who were attracted to California because of CIRM, UC San Diego, the Scripps Research Institute (TSRI), the Salk Institute, and the Burnham Institute decided to create a partnership that would bring together their distinctive expertise and resources to foster further collaborations in stem cell research. This was initially named the San Diego Consortium for Regenerative Medicine. Real estate mogul Malin Burnham, technology entrepreneur John Moores, and Qualcomm CEO Irwin Jacobs were instrumental in making the Consortium a reality and currently serve as Co-Chairs of the Board. All have been highly visible in their support for the Consortium, and have often been referred to as the "town elders". Smaller attempts at such collaborations, such as that by UC San Francisco and Stanford University to develop joint research/medical system, have interestingly failed. Difficulties such as cultural differences and disputes over ownership rights of scientific discoveries are only the beginning of the issues that arise with collaborations of this nature.

In May of 2008 the Consortium proposed to build a stem cell center, dubbed a “collaboratory” on the Torrey Pines Mesa within walking distance of the four partner institutions. The aim of the facility is to put many of those working on stem cell research under the same roof, with the hope that this will stimulate more creative outcomes. CIRM awarded a \$43 million grant to construct the 130,000 square foot facility, which was initially estimated to cost \$115 million. Rising costs have pushed the total to nearly \$130 million, creating a funding gap of approximately \$90 million. This gap is being filled through debt financing, to be serviced by the Consortium partners through rents paid by the research grants of those working in the facility. Groundbreaking for the facility occurred on March 29, 2010 and construction of the new facility is expected to be completed by July 2011.

The Consortium has quickly attracted outside interest. In September 2008, T. Denny Sanford, a wealthy businessman and philanthropist from South Dakota, announced a \$30 million donation to the Consortium, which is now called the Sanford Consortium for Regenerative Medicine. This was the second major donation Sanford made in San Diego as he previously donated \$20 million to the Burnham Institute so it could collaborate with Sanford Health of Sioux Falls. In February 2010, Sanford provided another gift of \$50 million to the Burnham Institute, now re-named the Sanford-Burnham Medical Research Institute. Through his first donation Sanford learned of the Consortium and, because embryonic stem cell research is illegal in South Dakota, he became interested in the work going on at the Institute. He said he was excited to support the unique collaboration because he believes that together the researchers can “quickly bring forward novel scientific developments that...help patients with limited or no treatment options today.”<sup>15</sup>

Since its creation, the California state program has awarded 295 grants totaling \$765 million. San Diego has received approximately \$230 million of that, amounting to roughly 30% of all funds. The Sanford Consortium has received nearly \$200 million of the San Diego awards. CIRM funding has also provided new resources and focus for hiring new faculty and researchers. For instance, UC San Diego’s Bioengineering Department chose to fill four new positions with researchers whose work relates to stem cells once the state funds were approved by voters.

In parallel, and in conjunction with the creation of research partnerships, other collaborative activities have taken place around stem cells, bridging the research and business communities. Among them is Stem Cells on the Mesa, an initiative hosted by the Sanford Consortium and managed by CONNECT in partnership with The Science Network. The effort is designed to bring together scientists to discuss a wide range of issues effecting stem cell research and innovation including ethics, business challenges, government policy, technological deficiencies, and collaborations. Since 2006, it has hosted annual conferences at which participants come together for a day of seminars on the latest breakthroughs in stem cell research. The

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<sup>15</sup> Russso Partners. *T. Denny Sanford Donates \$30 Million to San Diego Consortium for Regenerative Medicine*. Press Release. Sanford Consortium for Regenerative Medicine. 16 Sept. 2008.

conference also serves as a networking event, drawing not just academic researchers, but participants from the broader life sciences and business service communities. This is yet another example of the collaborative, cross-functional, and interdisciplinary networks that enrich San Diego's innovation economy.

### **5.6.2 Algae Biofuels – Can San Diego Become the “Green Houston”?**

Biofuels' importance to American energy policy has gone up and down since the 1960s, paralleling shifts in petroleum prices. Outside of the Oil Shocks of the 1970s and until the recent concerns about energy supplies and the threat of climate change, alternative energy has received scant attention. With today's renewed interest in alternative energy, the public, government, and investors are taking significant notice of alternative sources such as biofuels. The shift in awareness means San Diego's existing capabilities in oceanographic research and biotechnology place the region at the forefront of the new opportunities in algae biofuels, to the extent that some boosters are hoping to promote the region as a “green Houston”.

Though they are attracting a lot of public attention today, research and use of biofuels has been taking place for the past one hundred years. Despite a promising start, the use of peanut and vegetable oils in internal combustion engines was discarded for the cheaper and more available petroleum fuel by the 1920s. This reliance on petroleum continued well into the 1970s when the United States experienced its first oil shortages in relation to price increases on the Middle Eastern oil. Over the course of the decade, the US federal government launched several efforts to support research and development on alternative energy sources. Under President Carter, the Department of Energy initiated the Aquatic Species Program, the first effort to investigate the possible use of algae for energy production, which initially investigated the use of hydrogen within algae. After four years the program shifted its focus to research algae oil production. In the time that research was conducted, the Aquatic Species Program reported that it made “tremendous advances...in the science of manipulating the metabolism of algae and the engineering of microalgae production systems.”<sup>16</sup> Despite these advances, decreases in the price of oil and shifting federal R&D priorities resulted in the end of funding for this program. It was discontinued in 1996.

In the past couple of years, the US government has again turned its attention to alternative energy. Beginning in 2007, Congress renewed legislation related to renewable energy and fuel standards. In July of 2009, the Department of Energy announced that in the American Recovery and Reinvestment Act (ARRA), up to \$85 million would be for algae and advanced biofuels research and in January of 2010, the Department of Energy announced another \$78 million of funding for biofuel research and fuel infrastructure development.

While many of the federal biofuel research initiatives fluctuated in response to the changing price of oil during the 1970s and 80s, a handful of scientists at research institutions such as the

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<sup>16</sup> John Sheehan, Terri Dunahay, John Benemann, and Paul Roessler United States. *A Look Back at the U.S. Department of Energy's Aquatic Species Program—Biodiesel from Algae*. US. Department of Energy. Office of Fuels Development. 1998.

Scripps Institution of Oceanography (SIO) at UC San Diego and TSRI continued to work on algae research, although with an emphasis on marine sciences or plant biology rather than developing a new fuel source. This was due, in part, to there being more stable funding sources from other grant programs. Recent increases in fuel prices and new societal concerns about climate change, conditions outside of the research lab, have changed this. Venture capital began investing significant amounts into new biofuel companies and the US government increased the amount of funding devoted to energy research. Local scientists such as Stephen Mayfield, then at TSRI, Greg Mitchell at SIO, and Steve Briggs at UC San Diego, among others, who had become experts on algae and related fields, were now in a strong situation to shift the focus of their work towards creating viable biofuels.

Along with the academic community, San Diego companies began to capitalize on the revived interest in renewable energy, often building on the business and scientific capabilities found in the region's biotechnology cluster. In 2005 J. Craig Venter, who received his Ph.D. from UC San Diego, established the non-profit J. Craig Venter Institute and a for-profit company, Synthetic Genomics in La Jolla. Synthetic Genomics is developing several commercial applications utilizing synthetic biology, including the creation of biofuels. In 2009 Exxon Mobil, one of the world's largest oil companies, announced a multi-year, \$300 million agreement with Synthetic Genomics to conduct research on algae-based biofuels.<sup>17</sup> Another local algae biofuel company, Sapphire Energy, secured over \$100 million in venture capital financing during 2008. Sapphire's scientific advisors include Mike Mendez, Stephen Mayfield, and Steve Briggs. Given the location of the scientific talent, it was logical to establish the company in San Diego. The founding of other companies has quickly followed, including Kai BioEnergy and Biolight Harvesting, the former being founded by Steve Kay, a biologist who had previously worked at TSRI and is currently Dean of UC San Diego's Division of Biological Sciences.

There has also been overlap with the local defense industry. General Atomics and SAIC both secured awards from the Defense Advanced Research Projects Agency (DARPA) to develop a JP-8 jet fuel equivalent from algae. In January 2009, DARPA announced contracts worth up to \$43 million with General Atomics and \$25 million with SAIC, assuming all milestones are met. According to the San Diego Association of Governments (SANDAG), as of 2008, the county's algae biofuels industry was responsible for 513 jobs and over \$63.5 million in economic output for the San Diego region. Research alone on algae employs 272 scientists in the region.<sup>18</sup>

In a program produced by UC TV, Stephen Mayfield suggested that San Diego was the best place to move forward with research and development of algae biofuels because of two key factors: First, San Diego has a favorable environment for the growth of algae with lots of sunlight and warm temperatures. The second factor is that San Diego has a large quantity of biologists and a thriving biotech sector. Algae experts were already embedded in a community with a critical mass of biotech entrepreneurs. This meant that when the rest of the world

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<sup>17</sup> Synthetic Genomics press release, July 14, 2009. Available at <http://www.syntheticgenomics.com/media/press/71409.html>.

<sup>18</sup> SANDAG communication to Dr. Steve Kay, April 20, 2009.

developed an interest in alternative energy, San Diego already had the necessary infrastructure to quickly seize the new opportunity.<sup>19</sup>

In 2007 CleanTECH San Diego, a non-profit membership-based trade association, was incubated in CONNECT with the support of the City of San Diego and local cleantech companies. Now a freestanding entity, CleanTECH San Diego provides education, outreach, policy advocacy, and serves as a leader for further collaboration among the region's cleantech companies in an effort to accelerate San Diego's position as a world leader in clean energy. One such collaboration is with the Algal Biomass Organization, to advocate for the development and commercialization of algae biomass for biofuels and to provide networking and collaboration opportunities for researchers and companies in the field. CleanTECH San Diego helped to bring the annual Algae Biomass Summit in 2009 to town, and has partnered with a number of San Diego companies to apply for federal stimulus funding for renewable energy offered by the Obama administration, helping various community members connect and organize around this common cause. CleanTECH also frequently partnered with CONNECT and BIOCOM to present networking events and seminars related to market opportunities in the cleantech sector.

As federal R&D grants have become available for algae, members of the research community realize that to get biofuels to work, there needs to be a greater understanding of and the ability to manipulate algae. It is understood that there is a need to get research out of the lab and into commercial sectors in order for the research to potentially impact the environment. This requires interaction with all the other parties (engineers, biologists, farmers etc) in the biofuels innovation system. Researchers such as Steve Kay, Stephen Mayfield, and Greg Mitchell thus have brought together UC San Diego, TSRI and SIO in a collaborative effort to form the San Diego Center for Algae Biotechnology (SD-CAB). SD-CAB is designed to pool the resources and talent of researchers in a cross-section of technical fields to not only share ideas among the researchers, but to also better position them to receive research grants.

While there has been significant activity in San Diego's research and business communities around the algae biofuel opportunity, it is still early in this sector's development. Many science and engineering questions remain unanswered, which may be more effectively addressed by collaborative activities such as SD-CAB. However, several algae biofuel companies remain reluctant to share too many details for fear of compromising their competitive position. As the technology and industry mature, it is likely the firms will find pre-competitive or non-competitive issues on which to collaborate, such as standards and regulatory issues. Such an approach to growing this new industry cluster would mirror how other clusters have evolved in San Diego's recent history.

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<sup>19</sup> UC TV, "On Beyond: Algae Biofuels and Biotechnology with Stephen Mayfield, UC San Diego (Extended Interview)", Air date: January 6, 2010. Available at <http://www.uctv.tv/search-details.aspx?showID=18007>.

## 6. Possible Implications for Australia

Following our review of the development of San Diego's biotech industry, we pose several questions that may have implications for the growth of successful biotech clusters in Australia:

- Is there a sufficient understanding of collaboration as a social norm in innovative regions, as well as an understanding of the notion of “return on involvement”? This includes the willingness of regional stakeholders to work together to share key contacts, knowledge, access to resources, and in general, build the pre-transactional trust necessary for high risk endeavors such as those found in the biotech industry.
- Is there a strategy in place to build global centers of scientific leadership? Is there sufficient attention being paid to establish a few centers of global scientific leadership? Melbourne appears to have developed a reputation for high quality science. However, is this being leveraged for economic growth?
- Does Australia have the level of private sector involvement and risk-sharing that characterizes innovative regions such as San Diego and the Silicon Valley?
- Are there self-organizing innovation intermediaries that are perceived as honest brokers in the Australian biotech clusters? Many attribute San Diego's successful economic transformation to “bottom up” organizations like CONNECT and BIOCOM, which facilitated the growth of social networks and access to critical resources. In CONNECT's case, it benefitted from being based within UC San Diego for many years. This gave the organization a neutral position in the economy and enabled the creation of a bridge between the academic and business communities.
- Are there champions within the industry and within civil society who can play the kind of role people such as Bill Otterson, Malin Burnham, Irwin Jacobs, John Moores, and others have played in San Diego? These champions place community goals over individual company goals, and have frequently led regional efforts to develop new initiatives centered on cutting-edge technologies.
- How do Australia's emerging biotech clusters create communities that support risk takers and opportunity seekers without stigmatizing failure? Within San Diego, lessons learned are shared among entrepreneurs. Further, the initiatives and activities of organization like BIOCOM and CONNECT serve to help entrepreneurs minimize their mistakes and lower the risks associated with new endeavors.
- Might there be an opportunity for Australia to take advantage of the shift to a distributed partnership model of biotech business? A virtual model may create new opportunities for Australian companies as outside entities look to source new technologies and create new partnerships. This model is less tied to inputs being



concentrated in one location, which may reduce some of Australia’s challenges with geographic remoteness.

## 7. Appendix

### 7.1 List of Interview Subjects

- Richard Atkinson, President Emeritus, University of California (President 1995-2003); Chancellor, UC San Diego (1980-1995); Director, US National Science Foundation (1977-1980)
- Abigail Barrow, Director, Massachusetts Technology Transfer Center; formerly Managing Director, William J. von Liebig Center at UC SAN DIEGO; formerly Program Director, CONNECT
- Hon. Peter Beattie, Commissioner – Americas, Trade Queensland; Premier, Queensland (1998-2007)
- Barbara Bry, Associate Publisher & Executive Director, San Diego News Network; COO, Blackbird Ventures; formerly Director of Programs, CONNECT
- Malin Burnham, Chairman, Cushman & Wakefield
- Jerry Caulder, Executive Chairman, Finistere Partners; formerly CEO, Mycogen
- Charles Cochrane, founding scientist & Professor Emeritus, The Scripps Research Institute
- Shu Chien, University Professor & Chair, Institute for Engineering in Medicine, UC San Diego
- Kurt Chilcott, President & CEO, CDC Small Business Finance
- Pat Crowell, Attorney & Chief Counsel, General Atomics (ret.)
- John Davies, former Chair, UC Board of Regents
- David Doyle, Partner, Morrison & Foerster
- Peter Farrell, Founder & Chairman of the Board, ResMed
- Lisa Haile, Partner & Co-Chair, Global Life Sciences Sector, DLA Piper
- Robert Hamburger, Professor Emeritus and formerly Associate Dean, School of Medicine, UC San Diego
- Brent Jacobs, Senior Director, Global Life Sciences Practice Group, Cushman & Wakefield
- Wayne Kennedy, Sr. Vice President Emeritus, University of California; formerly Vice Chancellor for Administration, UC San Diego; formerly, Associate Dean, School of Medicine, UC San Diego
- Julie Meier Wright, President & CEO, San Diego Regional Economic Development Corporation; formerly Secretary of Trade and Commerce, State of California
- Gary Pace, Co-Founder, QRxPharma; Director, ResMed
- Joe Panetta, President & CEO, BIOCUM
- Duane Roth, CEO, CONNECT; Chairman & CEO, Alliance Pharmaceuticals

- Ivor Royston, Managing Member, Forward Ventures; founder, Idec Pharmaceuticals (now Biogen-Idec); founder, Hybritech
- Alan Trounson, President, California Institute for Regenerative Medicine
- Hon. Pete Wilson, Governor, State of California (1991-1999); United States Senator (1983-1991); Mayor, City of San Diego (1971-1982)
- Tim Wollaeger, Managing Director, Sanderling Ventures; formerly CFO, Hybritech

## 7.2 Interview Protocol

### Australian framework questions:

1. For a young person, not necessarily of Australian nationality, seeking a career in the biotech industry would you suggest they would be best off working in Brisbane, Sydney, Melbourne, or San Diego?
2. For a young Australian seeking a career in medical biotechnology, medical devices, or the ag-bio industry would you suggest that they would be best off working in Brisbane, Sydney, or Melbourne?
3. What have been the main historical drivers supporting the development of a biotech cluster in your region?
4. What have been the main impediments to biotech cluster formation in your region?
5. Does competition with other regional centers foster or inhibit clustering in biotechnology?
6. What are the main challenges you see for your organization or business over the next five years?
7. Over the next five years, what do you believe will be the most critical issues for the development of a cluster in your region and in your field of biotechnology?

### Role of government questions:

1. What role did government play in the development of the biotech industry, i.e. government policies such as direct funding, incentives such as tax credits, special initiatives? Which had the most impact?
2. Relative to other factors, such as industry self-organizing groups, availability of private risk capital, willing entrepreneurs, technically trained human capital, etc., how important was government's role?
3. Going forward, what is the appropriate role of federal, state, and/or local governments in supporting San Diego's biotech cluster?
4. Where is government an enabler and where is it a barrier?

### Challenge of remoteness questions:

1. Does San Diego's distance from political and financial centers affect the growth of the cluster positively or negatively?

2. What were some of the critical factors that helped the region manage its distance from key resources, such as capital, managerial talent, specialized business support services, manufacturing capabilities, etc.?
3. Is San Diego still considered to be far from key resources?

Questions related to major successes and flagship companies:

1. What do you consider to be San Diego's major successes?
2. How important are these outcomes to the cluster's development?
3. What about companies? Which are the big successes?
4. What role have they played in generating serial entrepreneurs, attracting and retaining talent and other companies, etc.?

Role of innovation intermediaries questions:

1. What are the key organizations that facilitate linkages between stakeholders and resources in the biotech cluster?
2. How do they accomplish this?
3. How valuable have these organizations been in helping the San Diego biotech cluster develop?
4. What were the key forces/factors affecting the development of these connections and boundary-spanning activities?
5. Do you see these organizations continuing to play a role in the community?

Role of university questions:

1. How would you characterize the role of the research institutions in San Diego (UC SAN DIEGO, Salk, Burnham, TSRI, etc.)?
2. Have there been challenges in getting faculty and researchers to become more interested in translational/applied research and commercialization versus basic research?
3. Why do you think UC SAN DIEGO, a major research and teaching institution, became involved in regional economic development?
4. How has UC SAN DIEGO interacted with other regional stakeholders (business leaders, investor community, government, etc.)?
5. What about technology transfer activities across the various research institutions? What works? What doesn't?

### 7.3 Summarized Interview Results For the Australian Framework Questions

For those that had knowledge of both San Diego and the three Australian regions, the comparative questions developed for the Australian survey were asked. Given the very small sample size of seven individuals and near similarity of the answers, the primary responses will be presented here rather than using the quantitative tables employed in the Australian Phase I Preliminary Survey.

In response to which location, Brisbane, Sydney, Melbourne, or San Diego, would be the best for a young person starting off in the biotech industry, the response was unanimously San Diego. Respondents noted that San Diego had a more mature, larger biotech industry, a more robust infrastructure in terms of facilities, research institutions, and business support services, greater access to capital, and a greater tolerance of risk. Some respondents were quick to note that this did not mean that the Australian regions were without merit or potential, but that the quality of the experience would be different in San Diego. A few stated that Australia's geographic remoteness was an impediment. Others felt that the country's isolation can be overcome by companies having a strong presence in the US market, while also taking a proactive approach to building partnerships with US companies.

When comparing Brisbane, Melbourne, and Sydney, the three regions were given different strengths and weaknesses. Contrary to the findings of the Australia survey results, Brisbane was perceived to be the best overall, given a more entrepreneurial culture there and a history of strong government engagement. Melbourne was noted to be the research leader and would make the best location for those seeking more research-oriented work. It was viewed as a close second to Brisbane, but while it had all of the assets, it was felt that things had not yet come together to sustain an entrepreneurial business culture. Sydney was noted to be the best location for medical devices, but perhaps had the weakest position as a biotech hub overall. A perceived lack of government leadership in Sydney and New South Wales perhaps has contributed to this.

Respondents stated that the main driver behind the growth of Australia's biotechnology clusters was the strength of the country's research institutions and high quality science. Respondents offered several views on the main impediments to cluster growth. These included the lack of indigenous venture capital, geographic remoteness from large markets, a cultural stigma placed on failure resulting in few serial entrepreneurs, and a lack of political leadership.

Despite the challenges, nearly all felt that the country had strong potential, and several offered suggestions for addressing the barriers. Remoteness could be overcome through proactive partnership development with non-Australian companies and placement of offices within large markets. Several also noted that the country was in a favorable geographic position to take advantage of the emerging markets in Asia, notably China. Partnerships with non-Australian firms and physical location within US and European markets may also increase the tolerance for risk among Australian entrepreneurs. In terms of the role of government, a few interviewees

expressed a strong desire for the renewal of the Commercial Ready Grant scheme. One interviewee went further and suggested that the government increase the R&D tax credit to 200% of expenditures, while also creating a privately-managed venture fund using two to five percent of the superannuation scheme. In addition to providing much needed capital to start-ups, it would also provide a valuable experience for those responsible for managing it.

#### 7.4 Federal R&D Funding to UC San Diego

Table 6 shows federal funding sources by agency. Table 7 provides a more detailed look at the sources of funding for UC San Diego’s health sciences programs.

**Table 6 UC San Diego Research Award Obligations by Major Agency, FY 2009**

Agency	Obligation Amount	% of Total
Department of Defense	\$103,634,829	11.8%
Department of Energy	\$13,570,962	1.5%
Department of Health & Human Services (which includes NIH)	\$365,580,706	41.5%
NASA	\$7,698,534	0.9%
NOAA	\$19,403,552	2.2%
NSF	\$90,626,758	10.3%
Misc. Federal	\$23,015,914	2.6%
<b>Federal Total</b>	<b>\$623,531,255</b>	<b>70.7%</b>
State of California	\$25,747,763	2.9%
Other Government	\$7,963,660	0.9%
Industrial	\$90,995,689	10.3%
Private Non-Profit (includes foundations)	\$133,386,230	15.1%
<b>Non-Federal Total</b>	<b>\$258,093,342</b>	<b>29.3%</b>
<b>Total</b>	<b>\$881,624,597</b>	

Source: UC San Diego Office of Contract and Grant Administration

**Table 7 UC San Diego Health Sciences Research Award Obligations by Agency, FY 2009**

Agency	Obligation Amount	% of Total
Department of Defense	\$51,161,685	5.8%
Department of Health & Human Services (which includes NIH)	\$292,055,007	33.1%
NSF	\$1,150,944	0.1%
Misc. Federal	\$204,736	0.0%
<b>Federal Total</b>	<b>\$344,602,372</b>	<b>39.1%</b>
<b>State of California</b>	<b>\$14,993,957</b>	<b>1.7%</b>
<b>Other Government</b>	<b>\$5,535,249</b>	<b>0.6%</b>
Business/Profit Entity	\$62,562,619	7.1%
Interest Group	\$20,502,113	2.3%
Foundation/Charitable Trust	\$2,971,875	0.3%
Other Charitable Organizations	\$21,850,335	2.5%
Higher Education Institutions	\$13,053,707	1.5%
Other UC Campus	\$8,207,013	0.9%
<b>Private/Industrial Total</b>	<b>\$129,147,662</b>	<b>14.6%</b>
<b>Health Sciences Total</b>	<b>\$494,279,662</b>	

Source: UC San Diego Office of Contract and Grant Administration

#### 7.4.1 Internal research funding allocation process

Within UC San Diego, there is a complex process for determining how resources are allocated to support the institution's mission of research and education. The most significant resource is people and the positions they fill. Positions are often referred to as FTEs (full-time equivalents). As a public institution, the university receives core operational support from the state, which includes resources to cover FTEs. FTE allocations at each campus are based upon a formula established by the state based on the number of student enrollments, but can be described a ratio of students to FTE positions. This ratio has fluctuated over time, depending on the state's budget and expected student enrollments, but has been in the 18 to 20 students-per-FTE range. How these FTE allocations are used is not directed by the state. Rather, those decisions are made by each UC campus at various levels within the hierarchy, from the Chancellor down through the Deans and Department Chairs. Each administrative level has discretionary funds at its disposal, which includes a mix of various sources, such as state funding, indirect cost recovery (overhead), and philanthropic gifts. Discretionary funds can be used to launch new programs or to hire new faculty or staff to enhance research capabilities in areas deemed to be a priority. This is often done when there is a perceived opportunity to bring in new research grants from the federal or state government. In one example noted earlier, the Bioengineering

Department chose to fill four FTE positions with experts in stem cells after California voters approved \$3 billion in funding for stem cell research.

The amount of discretionary money available decreases as one moves down the hierarchy, although science and engineering departments tend to have more discretionary funds to work with due to the large number of research grants they bring in. Because of this, the Chancellor may use his or her discretionary funds to support liberal arts departments to ensure the university offers a balanced curriculum. The university also has a budget committee that includes Vice Chancellors and representatives from the Academic Senate to review expenditures and discuss how future funds may be allocated across the institution.

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