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North Atlantic Innovative Relations of Swiss Pharmaceuticals and the Proximities with Regional Biotech Arenas

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Abstract: Under the pressure of increased global competition and processes of concentration, the pharmaceutical giants are reorganizing their innovative capacities. Technology and research and development (R&D) play a key role in the competitive strategies of multinational pharmaceutical companies. This article analyzes the interrelation of the far-reaching but spatially selective international expansion of R&D and technology of a major Swiss pharmaceutical company and its anchoring in regional arenas of innovation. It combines this international technological expansion with a perspective on integrating spatial and social proximities. Multinational corporations (MNCs) tend to locate their R&D activities in regions that are characterized by a richness of knowledge. The structure of inter- and intrafirm networks is shaped by the geography of talent. The Swiss pharmaceutical giants made substantial efforts to anchor themselves in regional arenas of innovation, such as the San Francisco Bay Area, Boston, and San Diego. A case study of a pharmaceutical giant's embedding in the biotech arena of San Diego reveals how oligopolistic rivals fight over privileged access to spatially concentrated bases of technology. MNCs attempt to create, complement, and substitute spatial proximity with other types of social proximities, internal as well as external to their own organizations. These efforts contribute to the generation of specific global-local interfaces in the processes of global scanning, transferring, and generating new pharmaceutical compounds and technologies.

Key words: pharmaceutical industry, biotechnology, multinational corporations, innovation.

The functions of research and development (R&D) are strategically among the most relevant sections of an enterprise in the pharmaceutical industry. At the same time, technology is a determining field for cooperation and competition among oligopolistic rivals. Large companies, particularly in the pharmaceutical industry, invest enormous sums on research. International localization of R&D and its interweaving occur in an extremely selective spatial manner; that is, highly innovative and technologically advanced pharmaceutical R&D takes place in only a few countries and regions of the world. This fact raises the question of the importance of regional and local economic and social contexts for the organization of the R&D functions of large companies. The highly selective localization of multinational corporations' (MNCs') research and technology capacities, as well as the associated problems of scanning, production, transfer, and use of technological knowledge, are the focus of this article. On the basis of a study of the pharmaceutical companies F. Hoffmann-La Roche (hereafter Roche) and

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Novartis (Ciba-Geigy and Sandoz before their merger in 1996), which have their headquarters in Basel, Switzerland, this article examines the interaction among the spatial concentration of research activities, their embeddedness in local arenas of innovation, and the interweaving of these activities on a North Atlantic scale.

The goal of this article is to contribute to the development of a concept of scales of innovative systems that combines international technological expansion by MNCs with all relevant dimensions of proximity. It aims to extend the understanding of the spatial implications of new innovative strategies in the context of oligopolistic rivalry in the pharmaceutical and biotech industries. The article combines theoretical approaches of oligopolistic rivalry and concentration of capital with those of regional innovative systems and emphasizes different aspects of proximity. It suggests the following two ideas:

1. Large pharmaceutical companies monitor technological developments on a global scale to internalize promising know-how and technologies. For this purpose, they enter into collaborative agreements with innovative biotech companies and research institutions that are generally clustered in specific regions. The search for talent and qualified people determines the location of new in-house capabilities. In view of the intensified oligopolistic rivalry for crucial technological potentials, large pharmaceuticals try to become anchored in regions from which they can launch an effective oligopolistic rivalry against their most important rivals.
2. To gain access to these localized technological potentials, large pharmaceutical companies strive to become insiders and to embed themselves in regional arenas of innovation that are characterized by specific social capital. On the basis of spatial proximity, they attempt to create a relational and cultural proximity to the key actors in these arenas of innovation. At the same time, they are forced to compensate for the lack in spatial proximity to other intrafirm research centers with organizational, relational, and virtual proximity.

This article is based, in part, on a comprehensive analysis of the internationalization of the Swiss pharmaceuticals Novartis and Roche (Zeller 2001b). It draws heavily on annual reports, media releases, industry reports, and articles in business and local newspapers. In addition, I conducted 19 semistructured interviews with senior executives and researchers on the internationalization of pharmaceutical R&D, and about 36 interviews on further corporate issues with biotech firms in the United States and Europe between September 1997 and March 2002. Also, I confirmed information by e-mail exchange with interviewees and other employees in research institutes.

The first section introduces the contradicting aspects of the recent discussion on international restructuring, the internationalization of technology, and the need for specific kinds of proximity. The second section illustrates the importance of regional arenas of innovation for the localization and organization of R&D by large companies. On the basis of the biotech arena of San Diego, it stresses the increasing importance of knowledge-rich regions for the strategic production of technology and the internalization of oligopolistic rivals. In contrast to the national and regional systems of innovation presented in the literature, I prefer the notion of arena of innovation (e.g., Lundvall 1992; Cooke 1998; Howells 1999; Archibugi, Howells, and Michie 1999). Thus, the focus is on *collaborating, rival,* and *conflicting* actors with collective and individual interests and cultures that exert different economic and politic power in specific socioeconomic contexts, not on elements and relationships that interact in the creation, diffusion, and deployment of new knowledge or regions as systems of collective order. The third section closes with reflections on the spatiality of innovative relations, of the generation and absorption of knowledge, and of oligopolistic corporate

technological strategies. The article contributes to the debate on relational perspectives of the firm-territory nexus (Dicken and Malmberg 2001).

Dimensions of Technological Flows and Proximities

Challenges for Corporate Strategies of R&D: Reconfiguring Scale

The changes in the relations among science, technology, and industrial activities since the end of the 1970s have entailed knowledge and technology increasingly adopting the character of strategic input and becoming a key factor of competitive advantage (Michalet 1985; Dunning 1993), particularly in the pharmaceutical industry (Taggart 1991, 236). Investments in R&D are among the most concentrated industrial expenditures in the world, in their distribution throughout both countries and companies. MNCs are the major actors in the technological race (Gerybadze and Reger 1999). The United States, Japan, Germany, France, Great Britain, Switzerland, Italy, and Sweden alone account for approximately 92 percent of the corporate pharmaceutical R&D expenditures worldwide (Pharmaceutical Research and Manufacturers of America (PhRMA) 2001, 80). The geographic distribution of the inventions of new active substances (NASs; new chemical and biological entities) displays a similar picture. Of the 211 NASs that were launched from 1996 to 2000, 81 were invented in the United States, 31 were invented in Japan, 22 were invented in Great Britain, 21 were invented in Germany, and 13 were invented in Switzerland (Verband Forschender Arzneimittelhersteller e.V (VFA) 1998, 33; 1999, 33; 2000, 33; 2001, 33).

The industry argues that it has faced a tremendous rise in R&D expenses and longer development times. The costs of R&D increased from about $120 million in the mid–1970s to about $231 million in 1987 (DiMasi, Hansen, Grabowski, and Lasagna 1991; DiMasi 1995). The Office of Technology Assessment (OTA 1993), using significantly higher opportunity costs, put the full capitalized costs of R&D per new drug at $359 million in 1990 dollars. DiMasi (cited in "Drug Companies" 2001) increased this figure to $802 million in 2000. These figures, based on data given by the industry, are strongly contested. Public Citizen, a U.S. consumer organization, calculated a figure of $150 million, on average, which does not include opportunity costs and state support for the industry's R&D efforts (see "Rx R&D" 2001).

In the same period, however, the lifespan of new products and technologies, as well as the exclusivity of the market, shortened (Mossinghoff 1995, 1,085; Drews 1998, 186; PhRMA 2002, 33). The industry faces a deficit of innovations. The number of NASs per year dropped from 86.2 in the early 1960s to about 40 in the past few years, although recent breakthroughs in genomics may increase the rate of innovation in the future (Grabowski and Vernon 1994; DiMasi 1995; Drews and Ryser 1996; Drews 1998, 204; Davis 1998; Shimmings 1999, 2000; Southgate 2001). Despite the recent remarkable growth rates in the pharmaceutical industry, especially in the United States, markets cannot be extended to the extent that is necessary to sustain continuous growth of the industry as a whole. In most countries, the industry faces growing market shares of generic drugs and greater pressure to contain health care costs (Schweitzer 1997; IMS 2000, 2002; PhRMA 2002).

Under the pressure of these challenges, the large pharmaceutical companies increased their research efforts and marketing expenditures. They reorganized their research departments repeatedly in the 1990s and implemented new forms of coordination and spatial configuration of their research sites. Massive rationalization efforts contributed to the reduction of the time and costs of development in this period (DiMasi 2001; Reinhardt 2001). After a significant geographic extension and trend toward the transnational configuration of R&D activities in the 1980s and early 1990s, globally active corporations have tended to consolidate and streamline their R&D organizations

since the mid–1990s (Gerybadze and Reger 1999). Because the huge capital requirements demand economies of scale, products must be launched in many markets simultaneously. These tendencies favor mergers and acquisitions and boost the internationalization process, since only large corporations are capable of raising the necessary funds. The degree of market concentration in individual therapeutic areas can be extremely high (Howells and Wood 1993, 41; Taggart 1993, 28ff; Organization for Economic Cooperation and Development (OECD) 1996, 84; Chesnais 1997, 166; Andreff 1996, 52; Drews 1998, 232; Zeller 2001b, 194ff). In the course of this process, there has been a rise in global oligopolies, which can be identified "as spaces of rivalry" among the rivals in the triad (Chesnais 1995, 1997). In the context of this increased oligopolistic rivalry, the large pharmaceutical companies attack their rivals in their home bases.

Technological Expansion of MNCs

Previous research showed a contradictory picture of the degree of internationalization of R&D and of technology. The internationalization of R&D expenditures was uneven in the individual industrial sectors in the late 1980s. The largest proportion of research activities abroad was conducted by companies in the chemicals, pharmaceuticals, and nutrition sectors (Pearce 1989, 12–20; Pearce and Singh 1992, 189). In their investigation of data on patents, Pavitt and Patel (1999) denied that R&D was being globalized and stressed the importance of the home base, claiming that high-tech industries are spatially more strongly fixed than are others. However, leading Dutch, British, Swiss, and Swedish MNCs had almost half or more of their R&D localized outside their home bases (Papanastassiou and Pearce 1994).

An exclusive focus on internal technology production presents an incomplete picture of the degree of internationalization, however, since both the location and dispersion of R&D and the degree of R&D cooperation and interweaving are important (Gassmann and von Zedwitz 1999). To understand the dynamics of internationalization, one needs to analyze the different dimensions of technology—the global use of technology, global technological cooperation, and the global production of technology (Archibugi and Michie 1995, 1997; Howells 1997, 14f). The variety of organizational forms and dimensions suggests that there may be different motives for internationalizing R&D, depending on the industry, the strategy, and the home base. Florida (1997, 101) determined that foreign MNCs locate R&D facilities in the United States mainly to gain "access to scientific and technical talent and developing links to the U.S. scientific and technical community." In their studies on foreign R&D in the United Kingdom, Pearce and Papanastassiou (1996, 322; see also Pearce 1999, 173) presented similar results with respect to pharmaceuticals and consumer chemicals. The "inward learning" requires presence at the most advanced locations (Gerybadze and Reger 1999, 255), which enables the fast transfer of local expertise into the company and internal diffusion to the appropriate places (Cantwell 1995, 171ff; Howells 1997).

According to Chesnais (1997, 170ff), five major dimensions of the international technological expansion and concentration of MNCs can be identified:

1. Internal technology production by MNCs: This dimension concerns the innovations that an enterprise generates within its own R&D capacities.
2. Acquisition of technology abroad with purchase or uneven power relations: Primarily MNCs, but also other enterprises and institutions, monitor technological developments and acquire specialized inputs from universities, public research centers, and small high-tech firms.
3. International exchange of know-how and technologies with cooperation and partnerships by means of strategic alliances. This dimension represents a form of oligopolistic acknowledgment

and the establishment of industrial entrance barriers.
4. Protection of knowledge and innovations abroad: The large enterprises individually protect their knowledge from imitation with patents abroad. The creation of international standards corresponds to a collective behavior of the companies.
5. Use of technological capital outside the country of origin or from a multinational base: This dimension includes three forms of international use of R&D activities: the production of goods for export on the basis of innovative products or processes; the sale of patent rights or transfers of licenses; and the use of technologies on the level of the entire company, which means that the technology circulates within the private sphere of the MNC.

The MNCs are the only actors that are active in all five dimensions. All other actors, such as mid-level and smaller enterprises, research institutes, or states, act only in two or three dimensions. The internationalization of R&D is also expressed by new types of organizational and network externalities (Gerybadze and Reger 1999, 255). The technological expansion is carried out over the exchange of materials and people. Whereas the transfer of knowledge that is embodied in materials normally does not raise major problems, knowledge embodied in human beings can be exchanged only by exchanging personnel. But the transfer of knowledge that is embedded in social capital is not possible because the networks that form this social capital remain locally fixed (Sölvell and Zander 1998).

Types and Dimensions of Proximity

Parallel to the debates on the internationalization of technology, the literature has discussed many approaches that emphasize the importance of regional industry and technology clusters for innovative processes. This literature has contributed arguments to explain the need for spatial clustering and proximity, such as transaction costs (Scott 1988); external economies of scale and scope—especially the pooling of labor markets (Krugman 1991); the reduction of uncertainty; collective learning processes and the cumulative nature of knowledge-based innovative inputs (Lundvall 1988); localized learning processes (Malmberg and Maskell 1997; Maskell and Malmberg 1999); the importance of tacit knowledge (Nelson and Winter 1982); and spillovers of knowledge and information from R&D in universities and industries (Feldman 1994). Colocation facilitates the saving of all kinds of transaction costs, rapid face-to-face interactions, and the monitoring of resources. Spatial proximity serves the emergence of "interpretative communities" that filter and transform "noise," rumors, impressions, and recommendations into valuable interpretations (Grabher 2001, 366–9). Furthermore, a high density of different institutions and various interactions between participants and institutions in a region are substantial requirements for the "local embeddedness" of large-company functions (Dicken, Forsgren, and Malmberg 1994).

Spatial concentration in itself does not create effective synergies. But spatial proximity facilitates cultural, organizational, and relational proximity; shared experiences; and perceptions in the sense of "untraded interdependencies" (Storper 1997, 35ff). Even Storper, an advocate of the "regional world," clarified that "noncosmopolitan knowledge" is not necessarily associated with spatial proximity but can also be settled in a technological, organizational, or professional space, such as an MNC. Yet regular human interaction is necessary in an interpretative and personal community. The problems of distance and the creation of proximity basically arise because firms need to overcome the disadvantages and to combine the advantages of concentration and dispersal (Schoenberger 1997, 21).

All five dimensions of technological expansion require and consist of social interactions. Although spatial proximity can be important, several kinds of social proximity must be considered to capture the scales of

innovative relations. Indeed, a company is confronted with completely different geographic levels of its own system of innovation. National, subnational, regional, and local innovation systems, and in addition to the mentioned geographic levels, sectoral innovation systems, need to be considered (Howells 1999, 72, 76). Therefore, in addition to *spatial proximity*, external and internal innovation relations are carried out on the basis of further types of proximity.

Institutional proximity (cf. Nelson 1988) refers to the institutional framework in countries and regions, such as legislative conditions, labor relations, business practices and accounting rules, dominant workplace practices, and the training system, which are all outcomes and elements of the evolution of political power relations that contribute to a "cultural affinity."

Cultural proximity is interrelated with institutional proximity and is expressed by a common cultural background, which facilitates the understanding of information and the establishment of norms of behavior between innovative actors and researchers (Lundvall 1988, 355). Social relationships among individuals, in the form of a common working ethos, a common language and culture, mutual knowledge, mutual trust, and mutually respected norms of behavior, form a common cultural space (Lundvall 1992, 47). The culture of specific, nationally rooted industrial practices can be incorporated into the design of products (Gertler 1995, 5; 1997, 52).

Within given institutional and cultural conditions, firms can create *organizational proximity* to compensate for the lack of spatial, institutional, and cultural proximity. Organizational proximity consists of shared organizational principles, rules, and codes, including a corporate identity and a corporate philosophy (Blanc and Sierra 1999, 196), to promote a certain coherence within a firm and compatibility among collaborating firms. It facilitates interactive and collective learning processes and the exchange of information, experiences, and knowledge (see also "organizational distance" in Gertler 1995, 5; 1997, 51). Organizational proximity simplifies interactive learning between users and producers (Lundvall 1993, 59). By creating their internal codes of information, MNCs generate a specific corporate culture that reduces national differences (cf. Lundvall 1992, 287). Actors that belong to the same space of relations (e.g., firms) interact according to adherence logic, whereas actors that are close in organizational terms, in that they have the same reference space and share the same knowledge, interact according to similarity logic (Torre and Gilly 2000, 174). The latter aspect refers to the context of institutional and cultural proximities.

However, every exchange within and among firms is based on personal relations. *Relational proximity* is expressed by informal structures that reinforce or counteract the effects of the formal organization. Knowledge, especially knowledge produced outside the firm, cannot be acquired, transferred, and transformed without continuing personal relationships (Sierra 1997, 25). An innovative firm must participate in the localized social capital. There are no hard monetary and value exchanges without soft relations or untraded interdependencies (Storper 1997, 38). Relational proximity is shaped by cultural affinity and facilitated by spatial and institutional proximity.

Technological proximity is based on shared technological experiences, bases, and platforms. It facilitates shared perceptions, as well as the anticipation of technological developments. Technological proximity facilitates the acquisition and exchange of technology. In the form of common standards and interfaces, it helps to erect entry barriers. Technological proximity depends mainly on institutional and cultural proximity and can be facilitated by spatial and relational proximity.

Virtual proximity can be produced by using communication and information technologies. An MNC can create virtual proximity to substitute partially for spatial proximity for a period of time on the condition that it disposes of organizational, cultural, and relational proximity among the members

of its network, to allow real communication to be established (cf. Howells 1995). Therefore, the effects of virtual proximity are limited.

Finally, a firm needs to manage *internal* and *external proximity* (Blanc and Sierra 1999). Internal proximity refers to the internal relations of a firm that should enable the creation and transfer of knowledge and technologies among different units and locations of the organization. Proximity to actors that are external to the firm serves the MNC's capability to scan and absorb externally produced knowledge and technologies. It helps to transfer internal resources to external partners.

The rounds of time-space transformation (Schoenberger 1997, 52) reduced the importance of spatial distance but did not ensure that distance was a solved problem. In innovative activities, the question of which organizational actors really need to be in constant contact and with whom is crucial. The constraints of a global oligopolistic rivalry have even increased the need for control over time and space. The challenge is this: To what extent are globally active companies able to overcome problems of spatial separation and to create, complement, and substitute different types of proximities and distances, internal as well as external to their boundaries? However, compared to other actors, they possess unique capabilities to handle this challenge. Every kind of information and knowledge is produced, transferred, and used in the context of specific combinations of proximities. The more tacit or uncodified parts of knowledge and trust are a relevant factor, the more important social interactions (Howells 1998), and therefore cultural and relational proximities, become. Transnational project teams, with their dense social interactions, can be an organizational instrument for creating such a specific mix of proximities (Zeller 2002a). The speed requirements in the pharmaceutical industry make the capability of creating and managing proximities an essential factor in oligopolistic rivalry. The connection of the dimensions of technological expansion, mentioned earlier, with a social comprehension of proximities provides a framework for analyzing the spatiality of innovative relations of MNCs.

Linking Innovation Hubs: San Diego and Basel

The Rise of Biotech Regions

In the course of the molecular-biological revolution and the emergence of biotechnology, the basic economic and technological conditions for the pharmaceutical industry changed considerably. In the late 1980s, a real boom started in the United States with the creation of biotech companies that were concentrated spatially in the San Francisco Bay Area, Boston, San Diego, Maryland–Washington, D.C., and New Jersey–New York (Willoughby and Blakely 1990; Blakely and Nishikawa 1992; Gray and Parker 1998; Prevezer 1998, 2001; Audretsch 2001).

The innovative process in the pharmaceutical industry has become so complex and diverse that even the largest pharmaceuticals are no longer able to cope alone with the important technological progress. Therefore, since the 1980s, they have developed strategies to acquire NASs and technologies through collaborations with biotech firms. Particularly in the United States, universities have increasingly also become partners of the pharmaceuticals (Gambardella 1995, 48–61; Drews 1998, 248). Collaborations with "big pharma" are a major financial resource for biotech companies in the United States. The share of financial inputs from partnerships with pharmaceutical and other biotech firms was 45 percent and 61 percent, respectively, in 1997 and 1998 but dropped to 14 percent in 2001, whereas, the share of venture capital oscillated from 1997 to 2000 between 4.7 percent and 7.9 percent and increased to 17.4 percent in 2001 (calculated from data from Burrill & Co. 1998, 1999, 2000, 2001, 2002). These figures also reflect the cycles of the stock markets and therefore the opportunities of initial public offerings and venture capital. But "big pharma" has

increasingly also installed its own venture capital funds to observe the technological developments. Given the numerous transatlantic collaborations between European pharmaceuticals and U.S. biotech firms, it is no surprise that the international transfer of technology in the biotech sector has played a particular role (see Pisano 1991; Dibner and Bulluck 1992; Valle and Gambardella 1993; Sharp, Thomas, and Martin 1994; Dolata 1996; Cavalla 1997).

Invasion and Embedding in California

The three Swiss pharmaceuticals have always localized their research establishments in specific regional knowledge-and-technology agglomerations. From the 1930s until the 1970s, the primary regional agglomeration, apart from the historical location of Basel, was in "pharmacy New Jersey," where these companies erected major research centers. In the 1980s, all three Basel companies began to invest heavily in biotechnology. Sandoz set up its own biotech research unit in its Basel headquarters in 1985. Shortly afterward, Ciba-Geigy and Roche also created biotech units. In the same period, the companies entered into collaboration agreements with the most advanced biotech firms, located primarily in the San Francisco Bay Area and the Boston region. Ciba-Geigy, Sandoz, and Roche became anchored with considerable investments in biotechnology and fixed capital in these two regions. Roche acquired a 60-percent stake in the biotech pioneer Genentech in South San Francisco in 1989 and two years later bought the revolutionary PCR technology (polymerase chain reaction) from Cetus in Emeryville, California, near Oakland, which was then immediately acquired by Chiron in Emeryville. Roche built up its PCR activities (Roche Molecular Systems) in Alameda, also near Oakland. In 1994, it took over the pharmaceutical multinational Syntex, including a big research center in Palo Alto. Roche reinforced its presence in the region when it acquired the German diagnostic and pharmaceutical company Boehringer Mannheim in 1998, which had localized its diagnostics works in Pleasanton and Berkeley. In addition, Roche entered at least a dozen collaborations with biotech firms that were based in the San Francisco Bay Area. About 5,000 people worked for Roche and for companies that were majority owned by Roche in the San Francisco Bay Area in 2000 (Woody 2000).

Sandoz and Ciba-Geigy also launched offensive localization and collaboration strategies in the San Francisco Bay Area (see Table 1). Sandoz took over 60 percent of SyStemix, located in Palo Alto, in 1991–92. SyStemix was fully integrated into Novartis in 1997. Ciba-Geigy entered a strategic alliance with the Emeryville-based Chiron, including a capital investment of about 47 percent, in 1994. Chiron was one of the largest and most dynamic biotech firms, with about 2,600 employees at that time (Chiron 1997a). In early 1997, Chiron had more than 1,400 agreements with universities and institutions and 64 collaborations with other firms (Chiron 1997b). Entering into these large alliances, Swiss pharmaceuticals simultaneously acquired a network of further collaborations and gained substantial access to the regional innovation resources. This embedding was completed by a multiplicity of research grants for university projects and further biotech collaborations in the San Francisco Bay Area (for collaborations in Boston, see Zeller 2002b).

The three companies have pursued the strategy of biotech alliances so systematically and rigorously that King and Moore (1995, 1) wrote, with some patriotic concern and admiration: "With direct or indirect stakes in more than 100 companies such as Genentech Inc. and Chiron Corp., plus near-exclusive access to research centers such as the Scripps Research Institute, the octopus-like Swiss have stealthily captured what may be the biggest foreign share ever of an emerging American technology." An analysis of Recombinant Capital's database of alliances confirmed that Roche and Novartis were the most active deal makers in the industry until the late 1990s (Hullmann 2000). Novartis Pharma increased its share

Table 1

Collaborations of Novartis with Biotech Companies (Including Ciba-Geigy and Sandoz) in the San Francisco Bay Area

Year	Partner	Deal
Ciba-Geigy		
1977	ALZA, Palo Alto	Acquisition of controlling stake of shares, collaboration in transdermal delivery systems
1981	ALZA, Palo Alto	Divestment of controlling stake, continuation of collaboration
1986	Chiron Corp., Emeryville	Joint venture "Biocine Company" in vaccines
1988	ALZA, Palo Alto	Ciba-Geigy Selfmedication acquires marketing rights for delivery technology
1990	Chiron Corp., Emeryville	Intensification of joint venture "Biocine"
1990	Genentech, South San Francisco	Development agreement together with Tanox (Houston)
1991	InSiteVision, Alameda	Several agreements in ophthalmics
1991	Chiron Corp., Emeryville	Research agreement in growth factors
1994	Chiron Corp., Emeryville	Broad-based strategic alliance ($2 billion), Ciba acquires 47.7 percent of the outstanding shares of Chiron and rights in combinatorial chemistry; Chiron has more than 20 collaborations with biotech and pharmaceutical firms, many of them in California
1995	Chiron Corp., Emeryville	Ciba acquires access to optical mapping and sequencing of genes, agreement in diagnostics
Sandoz		
Mid–1980s	ALZA, Palo Alto	Development of innovative drug delivery systems
1990	Protein Design Labs, Palo Alto	Research collaboration in anticancer antibodies
1991	Athena Neurosciences, South San Francisco (1996 acquired by Elan)	Exclusive license agreement for drug against spasms
1991	SyStemix, Palo Alto	Collaboration in immunology
1992	SyStemix, Palo Alto	Sandoz acquires 60 percent of outstanding shares, collaboration on stem cells and immunology
1992	Affymax, Palo Alto (1995 acquired by Glaxo)	Collaboration on catalytic antibodies
Novartis		
1997	SyStemix, Palo Alto	Acquisition of remaining 26.8 percent of shares
1997	Incyte Pharmaceuticals, Palo Alto	Development of a company-wide bioinformatics software for Novartis
1997	Affymetrix, Santa Clara	Novartis acquires access to *GeneChip* technology
1997	Titan Pharmaceuticals, South San Francisco	Novartis acquires worldwide marketing rights for Iloperidone
1998	Incyte Pharmaceuticals, Palo Alto	Extension of the agreement
1998	University of California–Berkeley	Novartis Agricultural Discovery Institute in San Diego acquires licensing rights
1998	Stanford University, Palo Alto	Research collaboration in transplantation technology
1999	Affymetrix, Santa Clara	Novartis Institute for Functional Genomics, Scripps Institute and Novartis Agricultural Institute, all in San Diego, acquire access to *GeneChip* technology
1999	Versicor, Fremont	Collaboration for the discovery of antibacterial active substances
1999	Rigel, South San Francisco	Five research projects for the identification of drug targets
2000	Axys Pharmaceuticals, South San Francisco	Genomics Institute of the Novartis Research Foundation in San Diego receives access to libraries in combinatorial chemistry
2001	Affymetrix, Santa Clara	Novartis Pharmaceuticals Corporation acquires access to *GeneChip* technology and customized gene sequencing and database information

Sources: Annual reports and media releases (cf. Zeller 2001b).

of the research budget for collaborations with external partners from 23 percent in 1997 to 27 percent in 2000, which was above the industry average (Herrling 2000). The embedding in these "new industrial spaces" does not mean that New Jersey and Basel had lost their importance. The Swiss pharmaceuticals made substantial research investments at these "old" locations, established new research centers in the early 1990s, and rebuilt research facilities in these years.

The increasing integration of Novartis into the region of San Diego and La Jolla, shortly following the embedding process in the San Francisco Bay Area, deserves a closer look. Ciba-Geigy and Sandoz had already been present in La Jolla and San Diego through several broad-based research collaborations since the early 1990s. The most important of these collaborations was the intensive ten-year research collaboration that Sandoz and The Scripps Research Institute (TSRI) entered into in 1992, which started in 1997. This long-term collaboration was designed to complement internal research programs in immunology, the central nervous system, and cardiovascular diseases (Rose 1992; Sandoz 1993, 17). It gave Sandoz the first right of refusal to technology developed at TSRI. It is not surprising that it provoked violent debates over the dependence of academic research on the interests of MNCs. Because of political pressure, the scope of the first agreement had to be reduced from $300 million to $200 million (Stern and Rose 1993; Holzmann 1993). Researchers at TSRI received the right to submit research proposals to Novartis. Finally, Sandoz acquired the right to commercialize 47 percent of TSRI's discoveries from 1997 onward (Rose 1994; Sandoz 1994). However, since then, this relationship has been extended several times. By forming this partnership, Sandoz became an important player in the fast-growing biotech milieu of San Diego. Beside the National Institutes of Health (NIH), Novartis is now the most important industrial financial contributor to TSRI. On the basis of early venture capital-induced contacts, local rival Ciba-Geigy began to cooperate with Isis Pharmaceuticals in the field of antisense technology in 1990. This collaboration was successfully resumed by CIBA Vision (Novartis's eye care division) until the introduction of Vitravene, a drug to treat AIDS-induced retinitis, in 1998. Other collaborations between Novartis and Isis are ongoing. Since the early 1990s, Ciba and Sandoz and their successor Novartis have made numerous further agreements with young biotech firms in San Diego and La Jolla (see Table 2).

San Diego/La Jolla probably has the highest concentration of biomedical research companies within walking distance. TSRI (founded in 1955) is one of the largest private, nonprofit research organizations in biomedical science in the United States. It houses some 2,800 staff, with 276 faculty members, nearly 800 postdoctoral fellows, 140 Ph.D. students, and nearly 1,500 technical and administrative support personnel. The neighboring Salk Institute for Biological Studies (founded in 1960), the Burnham Research Institute (founded in 1976), the University of California–San Diego School of Medicine (opened in 1964), and the Institute for Childhood and Neglected Diseases (founded in 2001) also employ several hundred researchers in biomedical science (Salk Institute 2002; TSRI 2002a). In 2001, the San Diego metropolitan area hosted about 100 biotech companies, 33 of which were publicly traded and 31 of which had 100 or more employees. All together, about 1,430 life scientists worked in the area in 1998 and about 11,000 employees worked in the broader pharmaceutical industry and life sciences research and development industry (Cortright and Mayer 2002, 16, 26, 29f).[1] UCSD CONNECT, founded

[1] Various reports have published different figures on firms and employees in the biotech sector. Cortright and Mayer (2002, 16) listed 94; Ernst and Young (2002) listed 110; Biocom, the local biotech lobby organization, listed almost 500 companies on their website (http://www.biocom.org/membership/membersearch.asp); and Porter and the Council (2001) listed 27,299

Table 2

Collaborations of Novartis with Biotech Companies in San Diego/La Jolla

Year	Partner	Deal
Ciba-Geigy		
1990	Isis Pharmaceuticals, Carlsbad	Antisense technology
1990	University of California–La Jolla	Arthritis, gene therapy
1992	Sibia, La Jolla, acquired by Merck & Co in 1999	Receptors aminoacids
1994	CoCensys, Irvine	Central nervous system, development and marketing
1994	Isis Pharmaceuticals, Carlsbad	Antisense technology: continuation and extension
1994	Isis Pharmaceuticals, Carlsbad	Antisense technology: continuation
1995	Isis Pharmaceuticals, Carlsbad	Antisense technology: continuation
1995	IDUN Pharmaceuticals	Cell death, signal transduction focus, central nervous system
1996	Neurocrine Biosciences	Multiple sclerosis drug
Sandoz		
1989	Cytel, San Diego	Research collaboration in immunosuppression
1991	Avalon Ventures, La Jolla	Foundation of venture firm, Avalon Medical Partners
1992	Allergan, Irvine	Collaboration in immunology
1992	Scripps Research Institute, La Jolla	Broad-based long-term collaboration
1995	Scripps Research Institute, La Jolla	Extension of broad-based long-term collaboration
Novartis		
1997	Neurocrine Biosciences	Continuation, Novartis terminated collaboration in 1999
1997	Biosite, Inc. Diagnostics	Novartis licenses antibodies to examine an immunosuppressive drug
1998	Molecular Simulations	Simulation technology for pharmaceutical development
1998	Trega Biosciences (acquired by Lion Biosciences, Heidelberg, Germany, in January 2001)	Combinatorial chemistry, obesity, diabetes
1998	CombiChem	Agrocultural research, combinatorial chemistry
1999	Diversa	Seeds, agricultural research
1999	Invitrogen Corp.	Functional genomics, cloning technologies, expression systems
2001	Immuosol	
Genomics Institute of the Novartis Research Foundation		
2000	LifeSpan Biosciences	GNF acquires access to GPCR database
2000	Molsoft (Molecular Software)	Joint research with GNF; GNF obtains access to database of Molsoft
2000	Salk Institute, La Jolla	Neuropeptide characterization
2000	The Scripps Research Institute	Osteoarthritis, central nervous system, stroke
2000	University of California–San Diego	Antidepressives
2000	University of California–Irvine	Ovarian cancer
2001	Syrrx, La Jolla	Five-year strategic alliance in structural proteomics (high-throughput protein structure determination)
2001	Sequenom	Creation of high-quality SNP (single nucleotide polymorphism) map of the mouse genome
2001	Xenogen	Imaging technology
2001	Immusol	Five-year oncology discovery and development, collaboration potentially worth $150 million
Chiron Corp., Emeryville (Novartis held 44 percent of the outstanding stock in 2000)		
1995	Viagene	Acquisition for $95 million, research in gene therapy
1998	Maxim Pharmaceuticals	Testing of Maxamine with Chiron's Proleukin

Sources: Annual reports and media releases (cf. Zeller 2001b).

in 1985, became an important institution that promotes the commercialization of scientific knowledge. It offers business advice and connects researchers with entrepreneurs and investors (Porter and the Council 2001, 69). In 2000, San Diego-based establishments attracted $681 million (TSRI alone received $132 million) from the NIH, which is the major funder of biotechnology in the United States. In 2000 alone, NIH disbursed $13.3 billion for research activities in the United States (Cortright and Mayer 2002, 14; TSRI 2002a).

Engagement in Genomics: Spatially Focused with North Atlantic Integration

In 1997, Novartis Pharmaceuticals decided to invest massively in the field of functional genomics and formed new research units in Basel and Summit, New Jersey, to integrate the latest findings from genome analyses into therapeutic concepts. Pursuing the goals of advancing on the technological forefront and combining all relevant technological achievements in-house, Novartis announced in April 1998 that it was going to invest about $250 million in a new genomics institute in San Diego (Novartis 1998a). After Novartis leased facilities in La Jolla for two years, the Genomics Institute of the Novartis Research Foundation (GNF) opened its new 260,000 square-foot building adjacent to TSRI in La Jolla in early 2002 (GNF 2002a).

This new research center, staffed with about 200 scientists and engineers, complements the other in-house functional genomics capability for therapeutic discovery. The GNF is one of the largest research institutes devoted entirely to functional genomics—a platform of technologies that aims to establish a functional relationship between a particular genotype and a given disease state. It is expected that this knowledge will help to identify new therapeutic targets (Dyer, Cohen, and Herrling 1999). Paul Herrling, global head of research at Novartis Pharma, explained the choice of location: "We already had this very good collaboration with Scripps. The question was how can I get these top shots I want. And our trick was that we and Richard Lerner [president of Scripps] offered dual appointments. They can work with us at the institute and can be professors at Scripps at the same time" (interview, 6 March 2001).

Novartis's relationship with TSRI and especially with TSRI's president Richard Lerner enormously facilitated Peter Schultz's recruitment as the director of the GNF. Schultz, a professor of chemistry at the University of California–Berkeley and a successful entrepreneurial scientist, received a parallel faculty appointment at TSRI. Previously, he was a founder of two technology companies, Affymax Research Institute (1988) and Symyx Technologies (1995). The recruitment of Schultz was highly important because it allowed Novartis to gain academic credibility and to create a close relational proximity to scientists and scientific communities.

Novartis launched additional, substantive investments. In autumn 1998, work on the Novartis Agricultural Discovery Institute in La Jolla began. This institute, designed to accommodate 180 researchers, is one of the largest research centers in the world that is dedicated to research on agricultural genomics. Novartis announced that it would invest $600 million over the next ten years to fund this huge initiative (Novartis 1998b). After the spin-off of the agribusiness and the subsequent merger with the agribusiness division of AstraZeneca in late 2000, this research center became part of the newly created company Syngenta and its international technology network, and its name was changed to Torrey Mesa Research Institute. Despite the obvious appeal of the location, the La Jolla City Council approved a tax-reduction package for Novartis that included a reduced property tax, conditional reductions in water and sewer fees, and rebates or credits based on additional-use taxes ("Novartis Tax Rebate Approved" 1999).

employees in the overall biotech-pharmaceutical cluster. Of course, political interests may account for the differences in these figures.

Despite an active collaboration strategy, Novartis concluded that the only way to converge the different technological strands and remain on the innovation front was to undertake huge internal efforts. The creation of an internal drug-discovery powerhouse was an indispensable prerequisite to the unfolding of a varied and successful collaboration strategy. The GNF's mission is focused on biological discovery and improved technologies for making those discoveries. The GNF aims to build a technology platform that will integrate all essential disciplines of the biological, chemical, engineering, and computational sciences that are important for the discovery of new drug targets and substances (McBride 2000; Schultz 2000b; GNF 2001, 2002a). Progress in functional genomics leads to the further miniaturization of the discovery process, with a huge increase in information that needs to be managed. These innovations promote the industrialization of drug-discovery research. The GNF underscored this tendency by employing an entire team of robotic engineers from General Motors.

The GNF consists of 14 scientific departments: Lead Discovery, Cancer and Cell Biology, Immunology, Neurobiology, Infectious Diseases, Cell Biology, Chemistry, Scientific Computing, Engineering, Cellular and Molecular Biology, Mouse Genetics, Protein Sciences, Genomics, and Information Technology (GNF 2002a). The hierarchy is flat. All departmental heads, as well as business development, legal issues, intellectual property, and finance functions, report directly to Schultz, the GNF director. The activities are structured in a three-dimensional matrix that is comprised of discovery, technology, and translational research (focused on the discovery of drugs). The organization can change rapidly. Several heads and scientists work in various groups. This organization is an attempt to create high levels of internal relational proximities and to facilitate the formation of shared project teams with external partners that favor external proximities.

The new research center in San Diego complements functional genomics research units in Basel and in Summit, New Jersey, with some 300 researchers.[2] The area of functional genomics is organized into seven operating units. The molecular biology laboratory and the model organisms and molecular cellular biology units are located in Summit, whereas the nucleic acid sciences, protein sciences, and transgenic sciences units operate in Basel. The employees of the life sciences informatics unit collaborate from both sites. The head of genomics and the person responsible for external collaborations are based in Summit–East Hanover. The three in-house genomics centers in San Diego, Basel, and Summit are the nodes of the internal genomics network. They collaborate with the Novartis research centers in Basel, Summit, Vienna, and Britain within specific therapeutic areas; with wholly owned Genetic Therapy in Gaithersburg, Maryland, in pharmacogenetics and gene therapy; and with wholly owned Palo Alto-based SyStemix in the fields of cell and gene therapy (see Figure 1). The most important external partners in genomics are the South San Francisco-based Affimetrix and Rigel; Celera in Rockville, Maryland; Incyte in Palo Alto; Protana in Odense, Denmark; the University of Maryland; GeneProt in Geneva; Genedata in Basel; Immusol in San Diego; and the SNP consortium[3] (Novartis 1999, 11; Vasella

[2] The merger of Ciba-Geigy and Sandoz into Novartis in 1996 brought together two huge R&D organizations with about 8,000 employees, operating in four large (two in Basel, one each in Summit and East Hanover, New Jersey), and seven medium-sized or smaller (Vienna in Austria; Horsham, London, and Cambridge in Britain; Takarazuka and Tsukuba in Japan; and Gaithersburg in Maryland) research centers.

[3] A consortium of pharmaceutical MNCs and other research institutions contributes to a public database of human gene markers called "single nucleotide polymorphism" (SNP). This genomics consortium in the United States and the European Union was formed in April 1999 by the Wellcome Trust, Bayer, BMS, Glaxo Wellcome (now GSK), HMR (now Aventis), Monsanto (now Pharmacia), Novartis, Pfizer, Roche, SKB (now GSK), and Zeneca (now AstraZeneca) (Novartis Pharma 1999).

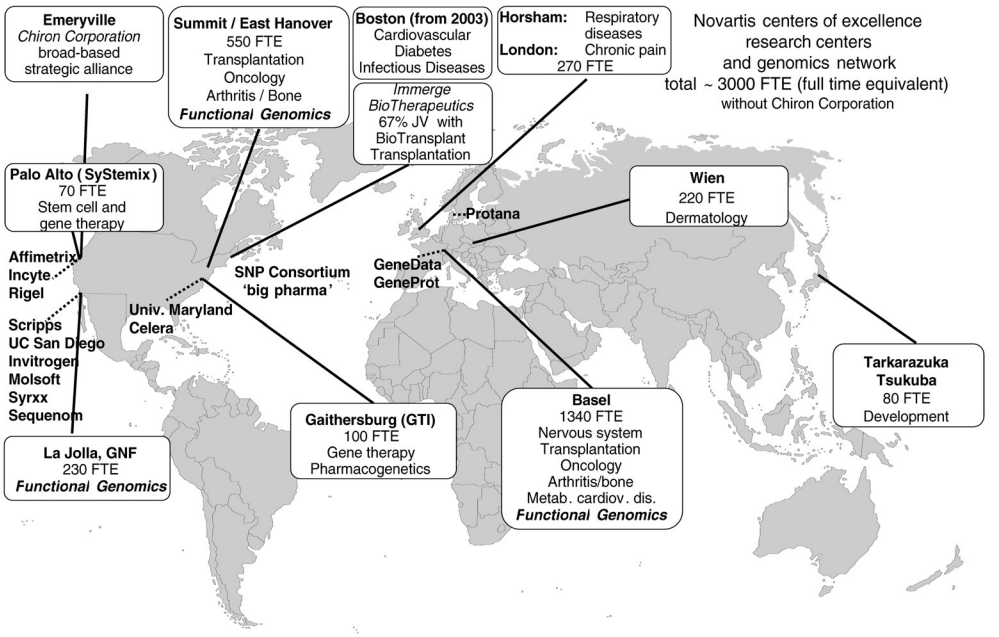


Figure 1. Novartis's centers of excellence, other research centers, and genomics network in 2002 (collaborations in other fields are not included).

1999; Herrling 2000; Schultz 2000b; Zeller 2001b, 460–64).

The GNF independently entered into several dozen further collaboration agreements in specific fields. The most important partners are listed in Table 3. Its direct neighbor, TSRI, remains by far its most strategic partner. In fact, the collaboration with TSRI has been highly productive for Novartis. By the end of 2000, the TSRI researchers had produced more than 2,000 manuscripts from the time the collaboration started, and Novartis owns the right to review the papers before they are submitted to journals. The collaboration also gives Novartis a priority right to file patents. This scientific know-how has shaped Novartis's research portfolio. It influenced seven already-terminated programs and contributed to the launching of seven new research programs until 2000 (Herrling 2000). To illustrate the partnering strategy, Herrling (interview, 6 March 2001) compared himself with a piano player. Every biotech firm represents a key of a piano and a large pharmaceutical company puts the piano together. "As a pharma guy who makes a therapy, I combine the keys and I play the music." But, the melody sounds harmonious only if a large company is able to manage the challenges of combining proximities and leveraging knowledge.

Complementing and Substituting External Proximities

Specific technology-based metropolitan advantages (*des atouts métropolitains*) are crucial for the emergence and reproduction of regional innovation arenas (Veltz 1996, 237ff). To minimize risks and uncertainty, firms tend to locate themselves in knowledge-rich metropolitan areas, mainly because they have relatively undefined expectations about the future as they search for a qualified workforce, knowledge pools, and specialist services. The same is true for workers and specialists. In an interview on 18 March 2002 in San Diego, Troy Wilson, GNF vice president of business development, clearly expressed this aspect: "We can recruit people now to GNF because they know that even if they are

Table 3

Import Partners of GNF's External Networks

Year	Partner	Deal
1999	Scripps (San Diego)	Broad-based research and academic alliance
1999	University of California–San Diego	Project-based collaborations
1999	Invitrogen (San Diego)	Functional genomics, cloning technologies, expression systems
1999	Affimetrix (South San Francisco)	GNF acquires access to *GeneChip* technology
2000	Axys (South San Francisco), acquired by Celera in 2001	GNF receives access to libraries in combinatorial chemistry
2000	Quantum Dot Corp. (Palo Alto)	Use of nanocrystals to develop biological assays for proteome analysis and gene expression at GNF
2000	Molsoft (San Diego)	Molsoft provides software for research in functional and structural annotation of new genomic sequences
2000	Lark Technologies (Houston)	GNF licenses high-throughput DNA sequencing technology
2000	LifeSpan (Seattle)	GNF acquires access to GPCR database
2001	Syrxx (San Diego), spin-off from GNF in 1999 with GNF director Peter Schultz on the board	Five-year strategic alliance in structural proteomics (high-throughput protein structure determination)
2001	Sequenom (San Diego)	Creation of high-quality SNP (single nucleotide polymorphism) map of the mouse genome
2001	Genicon Sciences Corp. (San Diego)	Multiyear partnership to use Genicon's proprietary Resonance Light Scattering technology
2001	Q3DM (San Diego)	Development of applications using Q3DM's high-throughput microscopy platform
2002	Libraria (San Jose)	Common identification of novel chemotypes that inhibit a kinease target
1999–	Australian National University, Mount Sinai, Oregon Brain Bank, Johns Hopkins University, Karolinska Institute, Stanley Foundation, Yale University, University of Chicago, Harvard Brain Bank, University of Virginia, Northwestern University, University of California–Irvine, University of California–San Diego, Tamagawa University, Kunming Institute, Peruvian Institute for Traditional Medicine, University of California–Los Angeles, Salk Institute	Many collaborations with universities in California and elsewhere in the United States, as well as with institutes in Europe, Asia, and South America

Sources: Company media releases and Schultz (2000b).

successful, they have many more opportunities here. And if they are not successful, they have still opportunities."

Legally, the GNF is part of a foundation. By implementing such a legally independent and organizationally relative independent status in respect to the headquarters, Novartis pursues two goals. First, it permits a culture to operate between "big pharma" and "small biotech." Schultz (2000a, 94) explained the advantages of such an organization:

> I retain my "academic" hat at the Scripps Research Institute. But the problem with academia is [that] it's very hard to focus resources like one can do in industry. On the other hand, companies sooner or later tend to become very product focused because they have shareholders wanting value. At this institute, we have the opportunity to have our cake and eat it, too. As we make discoveries or develop tools that have commercial value, we can pass on those discoveries through the foundation to Novartis, and they can use them to develop drugs; if Novartis isn't interested, we can spin off startups that can develop and apply the technology at a high level. The institute is free to continue developing new tools and making new discoveries. You can't do that in academia. You can't focus resources like that because it's a democracy, and everyone has a vote.

The second advantage is that this organizational and cultural distance to headquarters but closeness to the local research community facilitates joint projects with TSRI and the transfer of knowledge. Several key persons at the GNF besides Schultz hold joint faculty appointments at TSRI, which allows them to combine careers in industry and academia. For example, the microbiology group leader in the infectious diseases department of the GNF holds an appointment as an assistant professor in the Department of Cell Biology at TSRI (GNF 2002a). A considerable number of postdoctoral fellows at TSRI collaborate closely with the GNF. In Schultz's TSRI laboratory alone, one sixth of the listed postdoctoral fellows are either employed by GNF or have published articles with the GNF scientists (GNF 2002b; TSRI 2002b).

On the one hand, the establishment of numerous common project teams that include GNF and TSRI researchers, interns, and visiting scientists; the funding of doctoral and postdoctoral jobs at the local academic institutes; and joint appointments of faculty members and GNF department heads have contributed to the GNF's embeddedness in the local innovation arena. On the other hand, academics find it attractive to work in the GNF because GNF scientists have access to a wide range of opportunities at neighboring institutes: TSRI, Salk, Burnham, and the University of California–San Diego.

Schultz and the GNF played a decisive role in founding the Joint Center for Structural Genomics (JCSG) and the Institute for Childhood and Neglected Diseases (ICND). The JCSG is a consortium comprised of several research institutes in California, including TSRI, and is funded by the NIH (TSRI 2000). The ICND will act as an umbrella group within TSRI for young scientists who work in areas that are relevant to childhood diseases. The ICND closely collaborates with the GNF. Six faculty members opened the ICND, and three of the four new faculty are parallel department heads at the GNF (Benedyk 2001). This collaboration allows for many informal relations and shared projects, which are expressed, for example, by common authorship of a considerable amount of scientific articles.

The existence of the GNF is closely linked to the collaboration with TSRI. Compared to the University of California or Stanford University, which are seen as far too formal and rigid, TSRI is considered much more flexible and open to the penetration of corporate interests. As Wilson said in an interview on 18 March 2002:

> Scripps is a very flexible organization that is also run by a strong personality. . . . Berkeley is run as a democracy. So you have to get a committee to approve everything the university does. At Scripps and GNF, their approval is by one person. . . . We can make many things happen. Whether we have formal collaborations, we have many informal collaborations; you know, Scripps is the first place that we turn when we need expertise that is not in the GNF.

This close collaboration allows the GNF and Novartis to create remarkable relational, cultural, and spatial proximities to persons who are involved in localized innovation processes. Obviously, intellectual property issues are strategic. As Wilson put it:

> We have a certain number of informal collaborations. Novartis has rights to intellectual property generated from Scripps. They are similar to those, the intellectual property rights generated from GNF. So in many cases, the collaboration will be formed and be completed before we have a chance to catch up with it. They move that quickly. If we try to put up a written agreement in place every time, we kill the collaboration. Scripps is the only institution which allows this to happen. It only works because of that funding arrangement between Novartis and Scripps. If Novartis didn't have this evaluation right, then we would have to be much more formal. (Interview, 18 March 2002)

In its short history, the GNF has already spun out three technology-based companies—Syrxx in 2000 and Kalypsys and Phenomix in 2001—each of which successfully raised venture capital. These firms developed technologies that GNF and Novartis did not want to keep exclusively internal and that, by their very nature, will become obsolete after a few years. Novartis has an investment in each company. GNF director Schultz is a cofounder of Syrxx and is on the board of directors of all three companies. In the case of a successful development, Novartis and its BioVenture Fund can realize a considerable return on their investment. This spin-off strategy is another method of making GNF's boundaries permeable to the local scientific and business communities.

The GNF can be interpreted as a codification institution, absorbing and producing knowledge (including tacit knowledge) and technologies and transferring them to the internal corporate space of Novartis. Exposure in the local arena and the relative permeability of firm boundaries allows Novartis to use spatial proximity to local producers of knowledge to create relational, organizational, cultural, and probably even technological proximities. This is essential to promote innovative processes and a successful technological scanning. The creation of long-term relationships with major actors of the scientific community, the development of common experiences, and interpretative communities that permit the development of mutual trust are prerequisites for this kind of "innovative embeddedness" (cf. Grabher 2001).

Complementing and Substituting Internal Proximities

In a similar manner, internal organizational, cultural, and relational proximities are indispensable for managing the exchange of knowledge among the intrafirm research units located in San Diego, East Hanover–Summit, and Basel. Developing new technologies and methods, the GNF entered into dozens of collaborations with the Novartis research units in Basel, Summit–East Hanover, Horsham, and Vienna. These units provide knowledge about biomedical processes, diseases, and the concrete subjects for the application of theses new methods. The GNF is not integrated into the corporate structures like the other research centers and therapeutic areas. There is a direct reporting line from the head of GNF to the heads of research and of development of Novartis Pharma that underscores the high degree of organizational autonomy. A homogenization or a subordination of the GNF under the headquarter structures in Basel has to be prevented.

The collaboration and sharing of knowledge between the GNF and other Novartis research centers occurs on a project-by-project basis with the scientists directly involved, not with the heads of the therapeutic areas. Because of the GNF's technology-based profile, the counterparts on Novartis's research side are mostly the target platforms, technology platforms, and, to a much lesser degree, the discovery groups in the therapeutic areas (see Figure 2). This interaction is governed by steering committees in research, in development, and at the GNF. The exchange of information and codified knowledge normally does not raise major problems. However, to share tacit or uncodified *knowledge*, "you have to bring people personally. There is no other

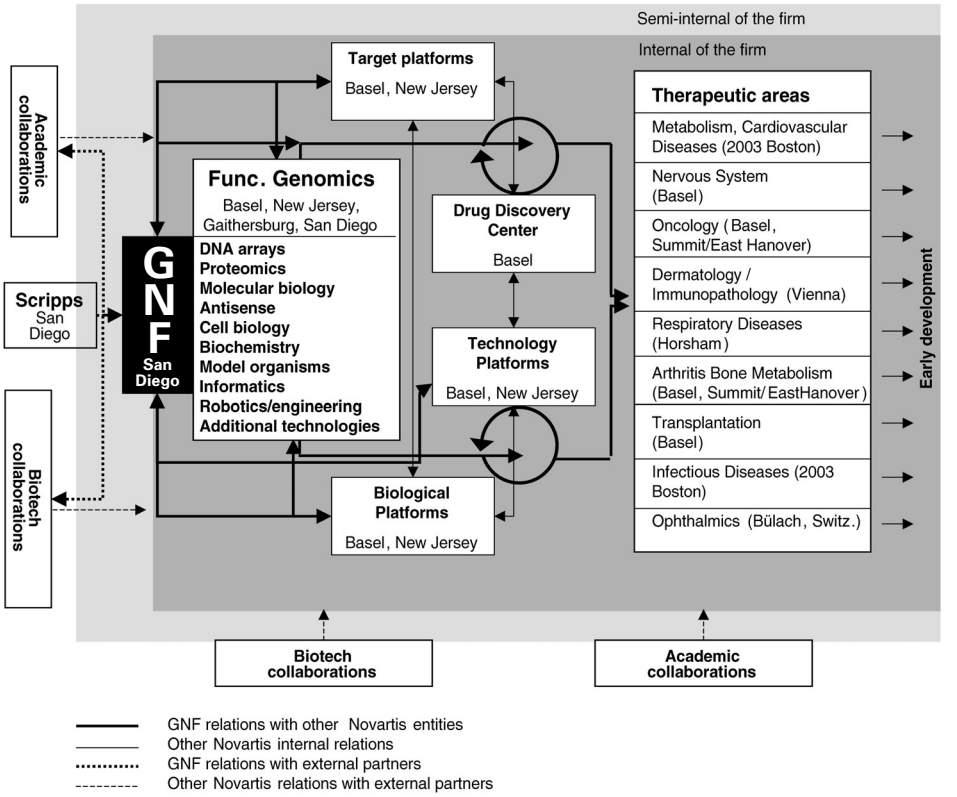


Figure 2. Intrafirm and extrafirm relations, knowledge, and technology flows of the Genomics Institute of the Novartis Research Foundation in San Diego in 2002.

way to do it" (interview with Wilson, 18 March 2002).[4] But international meetings are time consuming and costly. In addition, the promotion of personnel mobility among the major research centers through sabbaticals at the GNF and TSRI for researchers who work at other Novartis research centers helps to create these close relationships. And indeed, some of the best supporters within Novartis, among team leaders and senior scientists, have often visited the GNF or spent several months in La Jolla. However, the interviewees presented contradictory views on the importance of sabbaticals, which are limited and expensive.

Nevertheless, it remains a daily challenge to make these genomics groups' knowledge useful to other technology groups, especially in the application-oriented therapeutic areas. "And one of our single biggest problems, our single biggest issue we struggled with, is how to continue to increase the cooperation and collaboration with Novartis. That's our biggest problem," Wilson noted in an interview on 18 March 2002. In addition, the special position of the

[4] "You can't underestimate the face-to-face discussions, particularly the cultural differences and the beers in the bar after the meeting when people can talk freely," emphasized Alan Main, the former head of the Novartis research center in Summit, New Jersey, in explaining the problems involved in forming joint international project teams after the merger of Ciba-Geigy and Sandoz. No international team can be formed by communicating only with even the best electronic media because of misunderstandings caused by cultural and linguistic differences (interview with Main, 19 September 1997).

GNF within the Novartis organization raises culturally induced communication problems, especially in the transfer of intellectual property. "I think there is still a certain level of skepticism within Novartis that confidential information, in particular if it disseminates into GNF, would disseminate to the rest of the world," Wilson said.

Novartis-GNF relations show that a closer spatial proximity to innovative milieus can provoke problems in the internal organizational and technological proximities and capabilities. Therefore, an MNC has to manage the challenge of implementing an organization and strategy in a way that the internal organization is not constituted to the detriment of its external proximities, and vice versa. This dilemma reflects the increasing problems of coordination of locations, business units, and projects. Inward learning must be combined with internal processes of competence building and leveraging (Gerybadze and Reger 1999, 255).

Invasion of Oligopolistic Rivals

Overall estimations reveal that capital inflows by MNCs to a high-tech arena, such as the San Diego–La Jolla area, are important and can have cumulative effects. Large pharmaceutical companies have played a key role in San Diego's biotech industry. The region has attracted more than $1.6 billion in pharmaceutical-biotech research alliances since 1996 (Cortright and Mayer 2002, 24). Even though Novartis has been among the most active pharmaceutical giant in this region, almost all of the "top-ten" pharmaceuticals have substantial stakes in this region. Particularly, Pfizer after it acquired Warner-Lambert, with its recently integrated San Diego-based subsidiary Agouron Pharmaceuticals in 2000, has surpassed the rivals' local presence. It invested about $155 million between 2000 and 2002 for its expanded eight-building research center in La Jolla. Merck & Co transformed SIBIA Neurosciences, acquired in 1999, into Merck Research Laboratories. Johnson & Johnson has had a local presence for nearly 20 years and built a new biotechnology center in 1996 (see Table 4). Basel-based local rival Roche also maintains relations with several companies in San Diego. Thus, Roche acquired the marketing rights for Rituximab, one of the few products whose active substance was discovered in San Diego. IDEC Pharmaceuticals discovered this monoclonal antibody and developed it, together with Genentech and Roche, for the treatment of non-Hodgkin's lymphoma (IDEC Pharmaceuticals 1997; Roche 1997). The transatlantic flows of businesses and innovations between San Diego and Basel have been extended to small firms and spin-offs; for instance, San Diego-based Discovery Partners acquired Basel-based Discovery Technologies, a spin-off of Ciba-Geigy that is funded by the Novartis Venture Fund. In November 2001, this firm established its European headquarters in Basel (Discovery Partners 2000, 2001).

A particular method of technological scanning involves collaboration with venture capital firms. In 1991, Sandoz Pharma founded the joint venture Avalon Medical Partners at La Jolla with Avalon Ventures. Ciba-Geigy and Roche hold significant minority stakes in funds managed by Accel Partners and Advent International, respectively. These arrangements put all three companies in contact with start-up companies (Mehta and Isaly 1995; Zeller 2001b, 409, 432). Shortly after the merger in 1996, Novartis created the Novartis Venture Fund, which has financed numerous new biotech companies, many of them in Europe. It established the $100 million Novartis BioVenture Fund in 2000, which by February 2002 had invested in 13 biotech companies, mostly in the United States, 7 of which are in California and 4 of which are in San Diego County. In line with Novartis's technology scanning strategy, the BioVenture Fund moved its offices from Basel to the La Jolla-based GNF in November 2001 (Van Brunt 2002; Novartis Venture Fund 2002). This behavior of an individual corresponds to the general tendency of venture capital and research contracts to be highly concentrated within

Table 4

Invasion of Large Pharmaceuticals (Except Novartis and Roche) in San Diego

"Big Pharma"	Year	Investment
Eli Lilly	Early 1980	Lilly enters into collaboration with Scripps and gets right of first refusal for $50 million
	1986	Lilly acquires Hybritech (founded in 1978, the first biotech firm in San Diego) for $400 million and sold it a few years later; Lilly takes over the development of a diabetes medicine from Ligand Pharmaceuticals
	1996	Enters into collaboration with Neurocrine Biosciences
	2001	$200 million collaboration with Isis Pharmaceuticals
Schering-Plough (New Jersey)	1996	Acquisition of Canji gene therapy firm with late-stage clinical trials
Johnson & Johnson (New Brunswick, New Jersey)	1981	Johnson & Johnson enters into collaboration with Scripps
	1995	Acquires an 11 percent stake on Amylin Pharmaceuticals and extends collaboration in following years
	1995–99	Collaborations with Neurocrine Bioscienes
	1996	Creation of an integrated genomics-based research institute in a new 120,000-square-foot facility in La Jolla
	2002	Extension of existing research facilities
	2001	Collaboration with Maxia Pharmaceuticals
Warner-Lambert (Morristown, New Jersey) (acquired by Pfizer in 2000)	1999	Acquisition of Agouron Pharmaceuticals, which markets Viracept, an HIV medicine, for $2.1 billion; based on this drug, Agouron, founded in 1984, was the most successful biopharmaceutical company in the region with about 1,000 employees
Pfizer (New York, New York)	1991	Enters into research collaboration with Ligand Pharmaceuticals
	2000	Pfizer integrates Agouron in its global research and development organization after it acquired Warner-Lambert
	2002	Opening of the first part of an 800,000-square-foot research center in La Jolla, extending the site of Agouron (investment $155 million)
Merck & Co (Whitehouse Station, New Jersey)		Collaboration with Vical in fields of vaccines and gene therapy
	1999	Acquires publicly-held SIBIA Neurosciences
	2000	Transformation into Merck Research Laboratories; is heavily expanded and has about 120 employees
Elan Corporation (Dublin, Ireland)	1998	Enters into collaboration with Ligand Pharmaceuticals
	2000	Acquisition of Dura Pharmaceuticals for $1.590 billion; after a radical downsizing, Elan centralized its North American biopharmaceutical operations in Sorrento Valley, La Jolla; Elan has 8 collaborations with biotech companies
Chugai Pharma (Tokyo, Japan) (acquired by Roche in 2002)	1995	Establishment of Chugai Biopharmaceuticals in San Diego in 72-square-foot facility and over 100 employees
Sankyo Co. Ltd. (Tokyo, Japan)	1998	Establishment of the Sankyo Pharma Research Institute in San Diego

Sources: Kupper (1998, 1999b, 1999a), Crabtree (2000, 2002), Porter and the Council on Competitiveness and Monitor Group on the Frontier (2001), California Healthcare Institute (2002), Elan (2002), Johnson & Johnson (2002), Pfizer (2002a, 2002b), Chugai (2002), and Sankyo (2002).

a few metropolitan areas in the United States (Cortright and Mayer 2002, 22f).

In 2002, Novartis launched a similar process of oligopolistic striving for proximity to localized knowledge pools and to pharmaceutical rivals in the biotech arena of Boston. Madison, New Jersey-based Wyeth employs 800 people in its Cambridge, Mass. research laboratory, which originally belonged to the independent firm Genetics Institute. New Jersey-based neighbor and rival Merck & Co. began on 1 October 2001,

to build a large research center in Cambridge near Harvard Medical School that is designed for 400 scientists and administrative staff. The facilities are scheduled to open in 2004. On 6 May 2002, Novartis announced that it would lease laboratory facilities from MIT and would invest $250 million as a first step. The new Novartis Institute for Biomedical Research began operating in July 2003 and employs about 400 persons. Therefore, it recruited specialists even before Merck, and expansion could raise the number of employees to 900. As for the Genomics Institute in San Diego, Novartis recruited a renowned academic to lead the institute: Mark Fishman, formerly chief of cardiology and director of cardiovascular research at Massachusetts General Hospital. But the effects on the internal research organization will be even bigger because Fishman leads the global Novartis research organization from the new institute in Boston. The investments of Merck and Novartis are expected to influence the labor and real estate markets considerably (Krasner 2002; Merck 2001, 2002; "Novartis Opens Drug Research Center" 2002).

Conclusion

I draw three major conclusions: First, to generate and absorb knowledge, MNCs embed in knowledge-rich regions and reinforce the characteristics of a "pharma-biotech spider's web economy" in the context of the uneven development of capitalism. Second, MNCs strive for oligopolistic proximity, which reinforces the highly selective and fragmented geography of talent, innovation, and wealth. Third, a relational perspective that jumps scales and is based on democratic and social considerations must be developed.

Generation and Absorption of Knowledge

The spatial clustering of biotech firms and the increased importance of regional innovation arenas do not mean that innovative processes are more spatially integrated. Many input-output relations, innovative exchange processes, and shared processes in biotech R&D that are paralleled by large monetary transfers by no means happen in regionally integrated contexts (Oßenbrügge and Zeller 2002; Zeller 2001a). Rather one observes a combination of regional and nonregional input-output relations (cf. Markusen 1996).

Organizationally and geographically, flows of knowledge and technology occur extremely selectively. The spatial inequality and concentration have even been strengthened, although the proportion of R&D undertaken outside large pharmaceutical companies has increased. Also public spending, venture capital, and biotech firms tend to be highly selectively located. Big pharma is anxious to internalize externally produced local expertise; to diffuse it as quickly as possible internally to the appropriate places; and, at the same time, to externalize some of the inherent risks of all research processes. The entrepreneurial risk partially shifts toward the biotech firms that are transatlantically interwoven but that are nevertheless largely constrained regionally (e.g., they do not have development and marketing capacities). Amin and Thrift's (1992) characterization of "local nodes in global networks," as well as the somewhat harmonistic "regionalist" approaches and typologies of regional innovation systems (e.g., Cooke 1998), neglect the power hierarchies and interdependence among the oligopolistic rivals and the other actors in innovation arenas and the important role of the former in linking knowledge on a global scale.

The spatiality of this pharma-biotech spider's web economy is depicted in Figure 3. The technological competence is generated by actors who work in research centers and firms that together form an innovation hub and are spatially concentrated in a few knowledge-rich and economically wealthy regions. The socioeconomic context, consisting of collaborating and conflicting actors, forms the arenas and conditions for localized learning, and the processes of inclusion and exclusion. The MNCs structure and

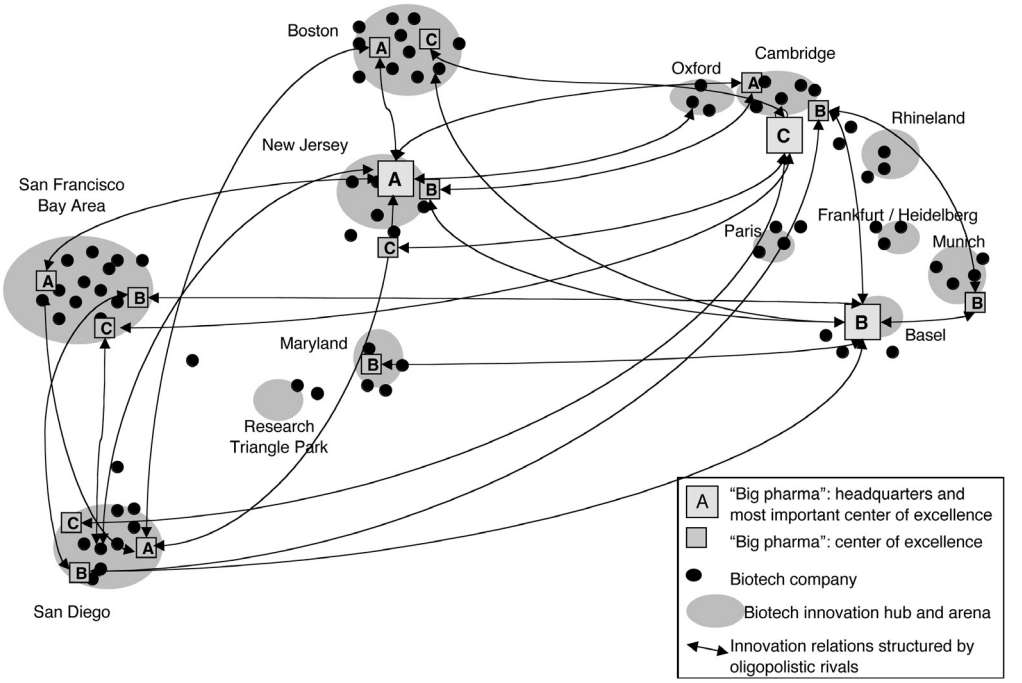


Figure 3. Innovation arenas, hubs, and nodes: Oligopolistic rivals A, B, and C with their headquarters and most important research centers, biotech companies, and innovation relations.

coordinate the innovative relations on transnational scales. They are the nodes that link knowledge and different strings of technology that are created in the arenas of innovation. They are the spiders that spin webs that, in most cases in the pharmaceutical and biotech industries, have a North Atlantic and sometimes a triadic extension. The spiders' weaving abilities depend largely on their ability to create, complement, and substitute spatial, organizational, cultural, relational, and technological proximities. That is, the technological expansion of MNCs also depends on the MNC's management of different proximities and distances. These interactions are a function of the MNC's capital and market power, which again are structured by the balance of power arising from the logic of the accumulation of capital and different actors' struggles on different scales (cf. Zeller 2000).

Novartis's partnership with TSRI and the embedding of the GNF into the local arena of innovation reveal that both before writing down contracts and based on mountains of contract documents, relational proximities and untraded interdependencies are created that enable the generation and transfer of tacit knowledge. In this sense, an important role of the GNF is to codify tacit knowledge that is bound in the social capital of the regional arena of innovative actors and its fruitful combination with other intrafirm knowledge (cf. Sölvell and Zander 1998). This example illustrates the cohabitation of tacit and codified knowledge within successive steps and rounds of production, acquisition, and transfer of both of them. Such stages of appropriation and learning are an evolutionary process (cf. Torre and Gilly 2000).

A pool of highly qualified labor promotes "relational assets," as well as the creation of uncodified knowledge and "untraded interdependencies," that make a region attractive (Storper 1997). However, it remains methodically unsolved how the specific effects and relevance of these "rela-

tional assets" can be seized. Novartis's engagement in La Jolla also reflects the ambition to tap, at least partially, into a business culture and social order that are considered industry friendly and that differ from its own cultural background of the European and Swiss chemical and pharmaceutical industries (cf. Schoenberger 1997, 119ff, 151ff). Creating such a cultural proximity serves to gain a better understanding of and to be relationally closer to what is happening in a part of the scientific front.

Oligopolistic Rivalry and Proximity

The oligopolistic rivalry among large pharmaceuticals occurs on a triad level, mainly on a North Atlantic scale. At the same time, rivalrous relations find their expression on other scales. Because of important differences in national markets, the outcome of oligopolistic rivalry is decided, to a considerable extent, by competition in national markets and by market shares in specific market segments. For this reason, European pharmaceuticals made huge efforts to strengthen their sales forces in the United States. Oligopolistic rivalry for technological potentials is translated into efforts to establish strong ties to innovation hubs and to become embedded in arenas of regional innovation. The existing and growing pool of knowledge in such arenas helps attract needed specialists from other regions. Attracting the best and brightest talent is crucial to the technology-and-innovation strategies of oligopolistic rivals in the pharmaceutical industry.

Investing heavily in fields of strategic technologies, MNCs not only absorb resources from regions, but, like investment and venture capital funds, they can pump enormous sums of externally accumulated capital and knowledge into a region. The oligopolistic rivals not only invade their rivals' sectoral and geographic markets, but also fight over privileged access to the spatially concentrated technological bases. Therefore, a large pharmaceutical company defends and expands its own technological base in the key regions, but it also strives to get a foot in the rivals' innovative systems. However, the mechanisms and cumulative effects of this geography of talent need to be further explored (see Florida 2001). A double mechanism of value capture can be observed. On the one hand, in the 1990s, there was a massive inflow of capital accumulated elsewhere to a few regions in the United States (Brenner 2002, 206ff). This inflow of capital helped extend the U.S. research and technological base. On the other hand, MNCs are eager to capture the values that are created in regional innovation arenas by highly specialized institutions, funded, to a large extent, by public institutions. Small companies are intermediate agents in this process. Part of these values is captured by financial organizations, such as venture capital funds, and pension funds. These processes reflect a strong rent-seeking behavior by MNCs and financial institutions (Chesnais 2001).

Striving for proximity to oligopolistic rivals is a major strategic behavior. This oligopolistic proximity is a highly conflictive form of proximity (cf. Blanc and Sierra 1999, 199). Such a process of regional and technological embedding extends Storper and Walker's (1989) geographic industrialization, in whose evolution a firm creates and shapes its own locational conditions. Because oligopolistic rivals adapt their strategies partly to those of their rivals and the number of biotech regions is limited, it is not surprising that many European, British, and New Jersey–New York-based large pharmaceuticals manifest similar spatial orientations to various innovation arenas.

Democratic and Social Relational Perspective

To understand both the spatial dimension of innovation relations and innovation systems and the spatial face of MNC's behavior, concepts need to be developed that are based on a dynamic understanding of interactions among different scales (cf. Swyngedouw 1997). I argue for adopting a relational understanding of space and territory. Approaches that are preconceived

on a specific spatial level (regional, national, and global) cannot capture the scalar dynamics of innovative relations and the jumping of scales by its protagonists (cf. Dicken and Malmberg 2001). The recent economic and political restructuring processes are linked with fundamental time-space transformations. These transformations are paralleled by the emergence of a growing number of untransparent and undemocratic institutions and processes, reduced citizenship rights, social disempowerment for some, and the growing influence and power of elites (Swyngedouw 2000, 551). Strong innovation hubs are based, to a considerable extent, on public investments in R&D and high-quality universities and research centers that frequently transfer knowledge. However, the shaping of these institutions and of the technologies that are produced in these institutions is out of democratic control. A democratic and social shaping of technological progress and its use needs to consider all scales of the production, exchange, and use of technology. The downside of technological arenas is widely marginalized and fragmented territories. Policies that are limited to winning regions cannot be a source of propositions that promote more democratic and more equal technological development.

References

Amin, A., and Thrift, N. 1992. Neo-Marshallian nodes in global networks. *International Journal of Urban and Regional Research* 16:571–87.

Andreff, W. 1996. *Les multinationales globales*. Paris: Éditions La Découverte.

Archibugi, D.; Howells, J.; and Michie, J. 1999. Innovation systems and policy in a global economy. In *Innovation policy in a global economy*, ed. D. Archibugi, J. Howells, and J. Michie, 1–16. Cambridge, U.K.: Cambridge University Press.

Archibugi, D., and Michie, J. 1995. The globalisation of technology: A new taxanomy. *Cambridge Journal of Economics* 19:121–40.

———. 1997. Technological globalisation and national systems of innovation: An introduction. In *Technology, globalisation and economic performance*, ed. D. Archibugi and J. Michie, 1–23. Cambridge, U.K.: Cambridge University Press.

Audretsch, D. B. 2001. The role of small firms in U.S. biotechnology clusters. *Small Business Economics* 17:3–15.

Benedyk, M. O. 2001. New institute within TSRI focuses on molecular genetics of disease. Researchers target illnesses of children and afflictions of people in developing nations. *Scripps News & Views* 1(2). Available online: http://www.scripps.edu/newsandviews/e_20010205/icnd.html

Blakely, E. J., and Nishikawa, N. 1992. Incubating high-technology firms: State economic development strategies for biotechnology. *Economic Development Quarterly* 6:241–54.

Blanc, H., and Sierra, C. 1999. The internationalisation of R&D by multinationals: A trade-off between external and internal proximity. *Cambridge Journal of Economics* 23:187–206.

Brenner, R. 2002. The boom and the bubble: The U.S. in the world economy. London: Verso.

Burrill & Co. 1998. 1998 quarterly press releases: First quarter. Available online: http://www.burrillandco.com/content_pr.html

———. 1999. 1999 quarterly press releases: Fourth quarter 1999. 1999 ends on a positive note for biotechnology. Available online: http://www.burrillandco.com/content_pr_99q.html

———. 2000. Second quarter 2000: Another busy quarter for biotech as the second quarter 2000 ends on a high note. Available online: http://www.burrillandco.com/content_pr_00q2.html

———. 2001. 2001 quarterly press releases. First quarter 2001: Biotech financing window closes amid a market downturn. Sequencing the human genome not enough. Available online: http://www.burrillandco.com/content_pr_01q1.html

———. 2002. 2002 quarterly press releases. Second quarter 2002: Biotech continues its downward spiral during Q2 02. Wall Street's enthusiasm wanes as investors wait for a turn around. Available online: http://www.burrillandco.com/ content_pr_02q2.html

California Healthcare Institute. 2002. Biomedicine: The next wave for southern California's economy. 2002 report on southern California's biomedical R&D industry. La Jolla, Calif.: California Healthcare Institute, PriceWaterhouseCoopers.

Cantwell, J. 1995. The globalization of technology: What remains of the product cycle model? *Cambridge Journal of Economics* 19:155–74.

Cavalla, D. 1997. Should biotechnology companies be based on research projects or niche technologies? *Drug News & Perspectives* 10:197–202.

Chesnais, F. 1995. World oligopoly, rivalry between "global" firms and global corporate competitiveness. In *Technological innovation, multinational corporations and new international competitiveness*, ed. J. Molero, 75–107. Reading, U.K.: Harwood Academic.

———. 1997. *La mondialisation du capital (nouvelle édition augmentée).* Paris: Syros.

———. 2001. La nouvelle économie: Une conjoncture propre à la puissance hégémonique américaine [The new economy: An economic cycle specific to the hegemonic power of the U.S.]. In *Une nouvelle phase du capitalisme?* ed. F. Chesnais, G. Duménil, D. Lévy, and I. Wallerstein, 41–70. Paris: Éditions Syllepse.

Chiron. 1997a. 1996 annual report. Emeryville, Calif.: Chiron Corporation.

———. 1997b. Chiron announces it will expand senior management by recruiting new chief executive officer. Media release, 29 January. Emeryville, Calif.: Chiron Corporation.

Chugai. 2002. Corporate, quick facts: Chugai pharma USA. Available online: http://www.chugaibio.com/corpinfo/corpinfo5.html

Cooke, P. 1998. Introduction: Origins of a concept. In *Regional innovation systems: The role of governance in a globalized world*, ed. H.-J. Bracyk, P. Cooke, and M. Heidenreich, 2–27. London: UCL Press.

Cortright, J., and Mayer, H. 2002. Signs of life: The growth of biotechnology in the U.S. Washington, D.C.: Brookings Institution.

Crabtree, P. 2000. Gene therapy thrives in San Diego County. *San Diego Union-Tribune*, 19 November, H7.

———. 2002. The new drug war: No quick cure as biotechs battle for premium space. *San Diego Union-Tribune*, 7 February, C1.

Davis, J. 1998. NAS in 1997: A good year for new launches. *Scrip Magazine* 1 (January), 60.

Dibner, M. D., and Bulluck, A. J. 1992. U.S./European strategic alliances in biotechnology. *Biotech Forum Europe* 9:628–35.

Dicken, P.; Forsgren, M.; and Malmberg, A. 1994. The local embeddedness of transnational corporations. In *Globalization, institutions, and regional development in Europe*. ed. A. Amin and N. Thrift, 23–45. Oxford, U.K.: Oxford University Press.

Dicken, P., and Malmberg, A. 2001. Firms in territories: A relational perspective. *Economic Geography* 77:345–63.

DiMasi, J. 2001. New drug development in the United States from 1963 to 1999. *Clinical Pharmacology & Therapeutics* 69:286–96.

DiMasi, J. A. 1995. Trends in drug development costs, times, and risks. *Drug Information Journal* 29:375–84.

DiMasi, J. A.; Hansen, R. W.; Grabowski, H. G.; and Lasagna, L. 1991. Cost of innovation in the pharmaceutical industry. *Journal of Health Economics* 10:107–42.

Discovery Partners. 2000. Form S-1 registration statement. Washington, D.C.: Discovery Partners International, Securities and Exchange Commission.

———. 2001. Discovery Partners International establishes European headquarters in Basel, Switzerland. Media release, 28 November. San Diego, Calif.: Discovery Partners International.

Dolata, U. 1996. *Politische Ökonomie der Gentechnik: Konzernstrategien, Forschungsprogramme, Technologiewettläufe* [Political economy of biotechnology: Firm strategies, research programs, technological competition]. Berlin: Edition Sigma.

Drews, J. 1998. *Die verspielte Zukunft: Wohin geht die Arzneimittelforschung*? [U.S. publication: Drews, J. 1999. *In Quest of Tomorrow's Medicines*. New York: Springer.] Basel: Birkhäuser.

Drews, J., and Ryser, S. 1996. Innovation. Deficit in the pharmaceutical industry. *Drug Information Journal* 30:97–108.

Drug companies must improve R&D efficiency to remain competitive. 2001. News release, 30 November. Boston: Tufts Center for the Study of Drug Development.

Dunning, J. H. 1993. Multinational enterprises and the global economy. Wokingham, U.K.: Addison-Wesley.

Dyer, M. R.; Cohen, D.; and Herrling, P. L. 1999. Functional genomics: From genes to new therapies. *Drug Discovery Today* 4:109–14.

Elan. 2002. 2001 Annual report & form 20-F. Dublin: Elan Corporation.

Ernst & Young, ed. 2002. Beyond borders. The global biotechnology report 2002. U.K.: Ernst & Young.

Feldman, M. P. 1994. *Geography of innovation*. Boston: Kluwer Academic Press.

Florida, R. 1997. The globalization of R&D: Results of a survey of foreign-affiliated R&D laboratories in the U.S.A. *Research Policy* 26:85–103.

———. 2001. *The economic geography of talent*. Working paper. Pittsburgh, Penn.: Heinz School of Public Policy and Management, Carnegie Mellon University.

Presented at the annual meeting of the Association of American Geographers, New York City, 1 March.

Gambardella, A. 1995. Science and innovation: The U.S. pharmaceutical industry during the 1980s. Cambridge, U.K.: Cambridge University Press.

Gassmann, O., and von Zedwitz, M. 1999. New concepts and trends in international R&D organization. *Research Policy* 28:231–50.

Genomics Institute of the Novartis Research Foundation. 2001. Discovery in the making. Available online: http://www.gnf.org/index.htm

———. 2002a. Genomics Institute of the Novartis Research Foundation. Available online: http://web.gnf.org/facilities.html

———. 2002b. Scientific Departments: Genomics Institute of the Novartis Research Foundation. Available online: http://web.gnf.org/scientific.html

Gertler, M. 1995. "Being there": Proximity, organization, and culture in the development and adoption of advanced manufacturing technologies. *Economic Geography* 71:1–26.

———. 1997. Between the global and the local. The spatial limits to productive capital. In *Spaces of globalization*, ed. K. R. Cox, 45–63. New York: Guilford Press.

Gerybadze, A., and Reger, G. 1999. Globalization of R&D: Recent changes in the management of innovation in transnational corporations. *Research Policy* 28:251–74.

Grabher, G. 2001. Ecologies of creativity: The village, the group, and the heterarchic organisation of the British advertising industry. *Environment & Planning A* 33:351–74.

Grabowski, H., and Vernon, J. 1994. Innovation and structural change in pharmaceuticals and biotechnology. *Industrial and Corporate Change* 3:435–49.

Gray, M., and Parker, E. 1998. Industrial change and regional development: The case of the U.S. biotechnology and pharmaceutical industries. *Environment and Planning A* 30:1757–74.

Herrling, P. L. 2000. Leading in the post-genome era. Paper presented at the media presentation on R&D Day, Basel, 6 December.

Holzmann, D. C. 1993. Healy rips Scripps' pact with Sandoz. *Bio World Today*, 12 March.

Howells, J. 1997. The globalization of research and technological innovation: A new agenda? In *Technology, innovation and competitiveness*, ed. J. Howells and J. Michie, 11–36. Cheltenham, U.K.: Edward Elgar.

———. 1998. Innovation and technology transfer within multinational firms. In *Globalization, growth, and governance*, ed. J. Michie and J. Grieve Smith, 50–70. Oxford, U.K.: Oxford University Press.

———. 1999. Regional systems of innovation. In *Innovation policy in a global economy*, ed. D. Archibugi, J. Howells, and J. Michie, 67–93. Cambridge, U.K.: Cambridge University Press.

Howells, J., and Wood, M. 1993. *The globalisation of production and technology*. London: Belhaven Press.

Howells, J. R. 1995. Going global: The use of ICT networks in research and development. *Research Policy* 24:169–84.

Hullmann, A. 2000. Generation, transfer and exploitation of new knowledge. In *Changing innovation in the pharmaceutical industry*, ed. A. Jungmittag, G. Reger, and T. Reiss, 71–96. New York: Springer.

IDEC Pharmaceuticals. 1997. Rituxan receives marketing clearance in first European country. Media release, 2 December, San Diego, Calif.: IDEC Pharmaceuticals.

IMS. 2000. Mergers—The drive to dominate: IMS health. Available online: http://www.ims-global.com/insight/news_story/0005/news_story_000517a.htm; . . ./news_story_000517b.htm; . . . /news_story_000517c.htm

———. 2002. World pharma sales 2001: U.S. still driving growth: IMS health. Available online: http://www.ims-global.com/insight/news_story/0204/news_story_020430.htm

Johnson & Johnson. 2002. Pharmaceutical research & development locations. La Jolla, Calif.: Johnson & Johnson Pharmaceutical Research & Development. Available online: http://www.jnjpharmarnd.com/locations/ca.html

King, R. T. J., and Moore, S. D. 1995. Swiss stakes: Basel's drug giants are placing huge bet on U.S. biotech firms. Roche, Sandoz, Ciba pay up, seeking breakthrough, a strategy some deride. *Wall Street Journal Europe*, 29 November, 1.

Krasner, J. 2002. Drug research giant heads to Cambridge. *Boston Globe*, 7 May, A1.

Krugman, P. 1991. *Geography and trade*. Cambridge, Mass.: MIT Press.

Kupper, T. 1998. A bitter pill. Without products to sell, San Diego biotechs rely heavily on funding from big companies for survival. But are they selling their future? *San Diego Union-Tribune*, 9 March, A1.

———. 1999a. Discovery adds third firm to group. *San Diego Union-Tribune*, 15 June, C1.

———. 1999b. N.J. health-care giant to buy Agouron. S.D. biotech reveals $2.1 billion deal. *San Diego Union-Tribune*, 27 January, A1.

Lundvall, B.-Å. 1988. Innovation as an interactive process: From user-producer interaction to the national system of innovation. In *Technical change and economic theory*, ed. G. Dosi, C. Freeman, R. Nelson, G. Silverberg, and L. Soete, 349–69. London: Pinter.

———. 1992. User-producer relationships, national systems of innovation and internationalisation. In *National systems of innovation: Towards a theory of innovation and interactive learning*, ed. B.-Å. Lundvall, 45–67. London: Pinter.

———. 1993. Explaining interfirm cooperation and innovation: Limits of the transaction-cost approach. In *The embedded firm*, ed. G. Grabher 52–62. London: Routledge.

Malmberg, A., and Maskell, P. 1997. Towards an explanation of regional specialization and industry agglomeration. *European Planning Studies* 5:25–41.

Markusen, A. 1996. Sticky places in slippery space: A typology of industrial districts. *Economic Geography* 72:293–313.

Maskell, P., and Malmberg, A. 1999. Localised learning and industrial competitiveness. *Cambridge Journal of Economics* 23:167–85.

McBride, G. 2000. Institute insight: The Genomics Institute of the Novartis Research Foundation. *Pathways: The Novartis Journal* 1:36–41.

Mehta and Isaly Healthcare Investments. 1995. Swiss company alliances. New York: Mehta and Isaly Healthcare Investments.

Merck. 2001. Annual report 2000. Whitehouse Station, N.J.: Merck & Co.

———. 2002. Annual report 2001. Whitehouse Station, N.J.: Merck & Co.

Michalet, C.-A. 1985. *Le capitalisme mondial* [World capitalism]. Paris: Presses Universitaires de France.

Mossinghoff, G. J. 1995. Health care reforms and pharmaceutical innovation. *Drug Information Journal* 29:1077–190.

Nelson, R. R. 1988. Institutions supporting technical change in the United States. London: Pinter.

Nelson, R., and Winter, S. 1982. *An evolutionary theory of economic change*. Cambridge, Mass.: Harvard University Press.

Novartis. 1998a. Novartis announces formation of the Novartis Institute for Functional Genomics. Media release, 8 April, Basel: Novartis International.

———. 1998b. Novartis announces USD 600 million investment in agricultural genomics. Media release, 21 July, Basel: Novartis International.

———. 1999. Geschäftsbericht 1998 [Annual report]. Basel: Novartis International.

Novartis opens drug research center in MIT's Tech Square. 2002. Media Release. *MIT News*, 6 May.

Novartis Pharma. 1999. Novartis jointly initiates consortium to create a public gene marker database. Media release, 15 April. Basel: Novartis Pharma.

Novartis tax rebate approved. 1999. *San Diego Union-Tribune*, 29 September, C2.

Novartis Venture Fund. 2002. Activity report 2001: Fostering entrepreneurial initiative in the life sciences. Basel: Novartis Venture Fund.

Oßenbrügge, J., and Zeller, C. 2002. The biotech region Munich and the spatial organization of its innovation networks. In *Technological change and regional development in Europe*, ed. L. Schätzl and J. Revilla Diez, 233–49. Heidelberg: Physica-Verlag.

Office of Technology Assessment. 1993. Pharmaceutical R&D: Costs, risks and rewards. Washington, D.C.: U.S. Government Printing Office.

Papanastassiou, M., and Pearce, R. 1994. La mondialisation de l'innovation et l'organisation de la R&D dans les multinationales [The globalization of R&D innovation and organization in the multinationals]. In *Les défis de la mondialisation: Innovation et concurrence*, ed. F. Sachwald, 69–106. Paris: Masson.

Pavitt, K., and Patel, P. 1999. Global corporations and national systems of innovation: Who dominates whom? In *Innovation policy in a global economy*, ed. D. Archibugi, J. Howells, and J. Michie, 94–119. Cambridge, U.K.: Cambridge University Press.

Pearce, R., and Papanastassiou, M. 1996. R&D networks and innovation: Decentralised product development in multinational enterprises. *R&D Management* 26:315–33.

Pearce, R. D. 1989. *The internationalization of research and development by multinational enterprises.* New York: St. Martin's Press.

———. 1999. Decentralized R&D and strategic competitiveness: Globalised approaches to generation and use of technology in multinational enterpises (MNEs). *Research Policy* 28:157–78.

Pearce, R. D., and Singh, S. 1992. *Globalizing research and development*. New York: St. Martin's Press.

Pfizer. 2002a. Pfizer: Global research and development. Available online: http://www.pfizer.com/pfizerinc/about/focus/research.htm

———. 2002b. California governor Gray Davis, Pfizer CEO Hank McKinnell and vice

chairman, John Niblack, Open Major Life Science Research Campus. Media release, 1 May.

Pharmaceutical Research and Manufacturers of America (PhRMA). 2001. *Pharmaceutical industry profile 2001.* Washington, D.C.: PhRMA.

———. 2002. *Pharmaceutical industry profile 2002*. Washington, D.C.: PhRMA.

Pisano, G. P. 1991. The governance of innovation: Vertical integration and collaborative arrangements in the biotechnology industry. *Research Policy* 20: 237–49.

Porter, M., and Council on Competitiveness and Monitor Group on the Frontier. 2001. *San Diego—Clusters of innovation initiative.* Washington, D.C.: Council on Competitiveness.

Prevezer, M. 1998. Clustering in biotechnology in the USA. In *The dynamics of industrial clustering. International comparisons in computing and biotechnology*, ed. P. G. M. Swann, M. Prevezer, and D. Stout, 124–93. New York: Oxford University Press.

———. 2001. Ingredients in the early development of the U.S. biotechnology industry. *Small Business Economics* 17:17–29.

Reinhardt, J. 2001. A broad innovative platform for sustained growth. Paper presented at media presentation on R&D Day, 30 October, New York.

Roche. 1997. *MabThera:* Hope for non-Hodgkin's lymphoma patients thanks to biotechnology. Media release, 28 November. Basel: F. Hoffmann-La Roche.

Rose, C. D. 1992. Alliance with drug firm assists Scripps research. *San Diego Union-Tribune*, 4 December, C1.

———. 1994. Scripps deal with drug firm approved. Sandoz is partner in scaled-back alliance. *The San Diego Union-Tribune*, 17 May, C1.

Rx R&D myths: The case against the drug industry's R&D "scare card." 2001. Washington, D.C.: Public Citizen's Congress Watch.

Salk Institute. 2002. The Salk Institute for Biological Studies. Available online: http://www.salk.edu/about.html

Sandoz. 1993. Geschäftsbericht [Annual report] 1992. Basel: Sandoz AG.

———. 1994. USA: Sandoz und Scripps schliessen Forschungsabkommen ab [Sandoz and Scripps enter research collaboration]. *Sandoz Bulletin* 30(106):36.

Sankyo. 2002. Company information, research institute. Available online: http://www.sankyopharma.com/research

Schoenberger, E. 1997. *The cultural crisis of the firm*. Cambridge, Mass.: Blackwell.

Schultz, P. 2000a. The Bell Labs of biology. *Technology Review* 103:94.

———. 2000b. Genomics Institute of the Novartis Research Foundation. Paper presented at media presentation Novartis Pharma R&D Day, Basel, 6 December.

Schweitzer, S. O. 1997. *Pharmaceutical economies and policy*. New York: Oxford University Press.

Scott, A. J. 1988. *New industrial spaces*. London: Pion.

Sharp, M.; Thomas, S.; and Martin, P. 1994. Transferts de technologie et politique de l'innovation: Le cas des biotechnologies [Technology transfer and innovation policy: The case of biotechnologies]. In *Les défis de la mondialisation*, ed. F. Sachwald, 155–212. Paris: Masson.

Shimmings, A. 1999. NAS in 1998: Quality not quantity counts. *Scrip Magazine* 1 (January):62–3.

———. 2000. NAS in 1999: Fierce marketing but fewer new products. *Scrip Magazine* 1 (January):68–9.

Sierra, C. 1997. Proximité(s), interactions technologiques et territoriales: Une revue [Proximities, technological and territorial interactions]. *Revue d'Économie Industrielle* 82(4th Quarter):7–38.

Sölvell, Ö., and Zander, I. 1998. International diffusion of knowledge: Isolating mechanisms and the role of MNE. In *The dynamic firm: The role of technology, strategy, organization, and regions*, ed. A. D. J. Chandler, P. Hagström, and Ö. Sölvell, 402–17. Oxford, U.K.: Oxford University Press.

Southgate, J. 2001. NAS in 2000: A bumper year for launches bucks the downward trend. *Scrip Magazine* 2 (February):80–1.

Stern, M., and Rose, C. 1993. NIH chief rips Scripps pact with Sandoz. *San Diego Union-Tribune*, 12 March, C1.

Storper, M. 1997. *The regional world: Territorial development in a global economy*. New York: Guilford Press.

Storper, M., and Walker, R. 1989. *The capitalist imperative*. New York: Basil Blackwell.

Swyngedouw, E. 1997. Neither global nor local: "Glocalisation" and the politics of scale. In *Spaces of globalization: Reasserting the power of the local,* ed. K. Cox, 137–66. New York: Guilford Press.

———. 2000. Elite power, global forces, and the political economy of "glocal" development. In *The Oxford handbook of economic geography*, ed. G. L. Clark, M. P. Feldman, and

M. S. Gertler, 541–58. Oxford, U.K.: Oxford University Press.

Taggart, J. 1993. *The world pharmaceutical industry*. London: Routledge.

Taggart, J. H. 1991. Determinants of the foreign R&D locational decision in the pharmaceutical industry. *R&D Management* 21:229–40.

The Scripps Research Institute (The Scripps Research Institute (TSRI). 2000. New genomic center funded to advance high throughput protein structure determination. Media release, 26 September. La Jolla, Calif: TSRI.

———. 2002a. About TSRI: Facts-at-a-glance. Available online: http://www.scripps.edu/intro/facts.html

———. 2002b. The Schultz lab/Schultz lab personnel and facilities. Available online: http://schultzweb.scripps.edu/personnel.asp

Torre, A., and Gilly, J.-P. 2000. On the analytical dimension of proximity dynamics. *Regional Studies* 34:169–80.

Valle, F. d., and Gambardella, A. 1993. "Biological" revolution and strategies for innovation in pharmaceutical companies. *R&D Management* 23:287–301.

Van Brunt, J. 2002. Corporate VCs keep an eye on the future. *Signals Magazine: Online Magazine of Biotechnology Industry Analysis*, 3 May:14.

Vasella, D. 1999. Novartis building on strong fundamentals. 1998 Novartis Financial Results Press Conference, 16 March. Basel: Novartis International.

Veltz, P. 1996. Mondialisation, villes et territoires. l'Économies d'archipel [Globalisation, cities and territories. Economies of archipelago]. Paris: Presses Universitaires de France.

Verband Forschender Arzneimittelhersteller (VFA). 1998. Statistics 98: Die Arzneimittelindustrie Deutschlands [German Association of Research-Based Pharmaceutical Companies]. Bonn: VFA.

———. 1999. Statistics 99: Die Arzneimittelindustrie Deutschlands [German Association of Research-Based Pharmaceutical Companies]. Bonn: VFA.

———. 2000. Statistics 2000: Die Arzneimittelindustrie Deutschlands [German Association of Research-Based Pharmaceutical Companies]. Berlin: VFA.

———. 2001. Statistics 2001: Die Arzneimittelindustrie Deutschlands [German Association of Research-Based Pharmaceutical Companies]. Berlin: VFA.

Willoughby, K. W., and Blakely, E. J. 1990. *The economic geography of biotechnology in California: An exploration of regional form and advanced technology industries.* Berkeley: Institute of Business and Economic Research, University of California– Berkeley.

Woody, J. 2000. "Erfolg dank unseres langjährigen engagements" [Success owing to our commitment of many years]: Interview with James Woody, general manager of Roche Palo Alto. *Roche Magazin* 66(December):24–6.

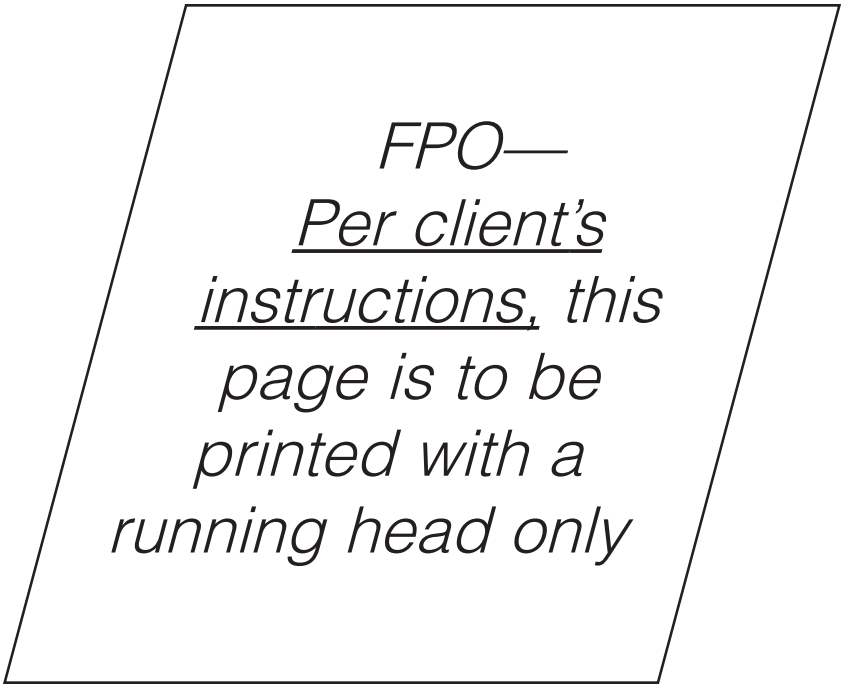
Zeller, C. 2000. Re-scaling power relations between trade unions and corporate management in a globalising pharmaceutical industry: The case of the acquisition of Boehringer Mannheim by Hoffmann-La Roche. *Environment & Planning A* 32:1545–67.

———. 2001a. Clustering biotech: A recipe for success? Spatial patterns of growth of biotechnology in Munich, Rhineland and Hamburg. *Small Business Economics* 17:123–41.

———. 2001b. *Globalisierungsstrategien—der Weg von Novartis* [Globalization strategy—The way of Novartis]. Berlin and New York: Springer-Verlag.

———. 2002a. Project teams as means for restructuring research and development in the pharmaceutical industry. *Regional Studies* 36:283–97.

———. 2002b. Regional and North Atlantic knowledge production in the pharmaceutical industry. In *Knowledge—The spatial dimension*, ed. V. Lo and E. Schamp, 131–66. Münster: Lit-Verlag.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