

**INTER-FIRM R&D PARTNERING IN PHARMACEUTICAL BIOTECHNOLOGY
SINCE 1975: TRENDS, PATTERNS, AND NETWORKS**

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Abstract

This paper analyses a large, longitudinal database on inter-firm R&D partnerships formed in the high-tech pharmaceutical biotechnology industry since 1975. Our research indicates an overall growth in the number of annually, newly established R&D partnerships where research partners consistently prefer contractual partnerships to equity-based alliances. In the networks that develop through these R&D partnerships, small, entrepreneurial biotechnological companies take a leading role during the 1980s when biotechnology first became relevant for the pharmaceutical industry. The 1990s, however, show a different pattern with established, large pharmaceutical companies becoming more dominant, acting as nodal players with multiple partnerships with a variety of other companies.

INTRODUCTION

The main purpose of this paper is to present an overview of major long-term trends and patterns in R&D partnering between companies that operate in the high-tech pharmaceutical biotechnology industry. In that context, we study pharmaceutical biotechnology R&D partnerships formed by all companies active in pharmaceutical biotechnology, a population that consists mainly of large pharmaceutical companies, diversified chemical companies and a range of dedicated biotech companies. The starting point for this analysis is the mid-1970s, when pharmaceutical biotechnology was still at its very early stage of both technological and commercial development. We will follow the development of this emerging sector of industry until the end of the 1990s. The main data source for our analysis is the MERIT-CATI database (see appendix I).

After we present an overview of general trends in R&D partnerships, which demonstrates a somewhat cyclical growth pattern in the number of newly established partnerships, we will discuss some interesting features of major modes of research cooperation between companies. Traditionally, high-tech companies have preferred to use equity joint ventures as a major mode of cooperation, but gradually they have started to experiment with other forms of cooperation. For pharmaceutical biotechnology, we will look at some trends in the choice that companies make with regard to several modes of research cooperation, such as R&D joint ventures, minority holdings, R&D agreements, and research contracts.

In the next section, we will discuss some major changes in the structure of research partnering networks over time, examining both network-level characteristics and partnering behavior at the level of individual firms. This part of the analysis first concentrates on the representation of actual inter-firm R&D networks formed during five periods of five years, beginning with the period 1975-79 and ending with the period 1995-99. It presents an

intriguing story of networks that are gradually becoming more and more complex, starting as isolated pairs of cooperating companies with a few small clusters of multi-partner networks developing into a very dense, interrelated, large network with a multitude of companies.

When we analyze the role played by individual companies, we will concentrate on both large, established pharmaceutical companies and relatively small, entrepreneurial biotechnology firms that are known for having played a crucial role in the development of pharmaceutical biotechnology (see e.g. Arora and Gambardella, 1990; Barley, Freeman, and Hybels, 1992; Pisano, 1991; Powell, Koput, and Smith-Doerr, 1996; Roijakkers, Hagedoorn, and van Kranenburg, 2005). Our analysis will get a clear Schumpeterian flavor when we examine the role of both groups of companies and their individual ‘representatives’ in the changing networks of inter-firm R&D partnering throughout the sub-periods that we study.

In the final section, we will draw some conclusions regarding the main topics of this paper. A number of appendices describe our data and data sources, our own network visualization software tool, and the list of companies and their labels that feature in the networks that we analyze.

GENERAL TRENDS IN R&D PARTNERSHIPS SINCE 1975

Historical growth pattern

Previous research (see amongst others Chesnais, 1988; Hagedoorn, 2002; Hergert and Morris, 1988; Hladik, 1985; Mariti and Smiley, 1983; OECD, 1986, 1992) has established that, after a small growth in the number of inter-firm partnerships made during the 1970s, the formation of these partnerships did not really take off until the beginning of the 1980s. We also find this particular growth pattern for the group of partnerships studied in this paper, i.e. pharmaceutical biotechnology R&D partnerships. Figure 1 shows the particular trend in the

formation of newly established R&D partnerships in pharmaceutical biotechnology as well as the growth in overall partnering activity during the period 1975-1999.

-----Insert figure 1 about here-----

During the second half of the 1970s, the number of newly established pharmaceutical biotechnology R&D partnerships, as found in the MERIT-CATI database, remained at a very low level of between a few to about 10 partnerships made each year during most of that period. Figure 1 also indicates that R&D partnerships formed by companies active in pharmaceutical biotechnology account for a very small share of the total number of partnerships (less than 6%) made during the last couple of years of the 1970s.

During the first half of the 1980s, there is a gradual increase of the number of newly established R&D partnerships from fewer than 20 pharmaceutical biotechnology partnerships in 1980 to about 40 agreements in 1984. This particular growth pattern continues well into the second half of the 1980s, ultimately reaching a high level of around 65 partnerships made in 1986. The last couple of years of the 1980s show a substantial drop in the newly established R&D partnerships to slightly over 30 pharmaceutical biotechnology alliances in 1989. If we examine the overall trend in the total number of newly established R&D partnerships formed during the 1980s, it is obvious that this number increases more rapidly than the number of newly established pharmaceutical biotechnology partnerships. In relative terms, the share of biotechnological partnerships in total alliance activity has increased somewhat to more than 10% of all alliances in the late 1980s (see figure 1).

During the early 1990s, the number of newly established pharmaceutical biotechnology alliances drops even further to fewer than 20 R&D partnerships in 1990 after which this number takes off again to reach a high level of about 170 partnerships in 1996. At

the end of the period of our analysis, the number of newly established partnerships is decreasing again to slightly over 100 alliances in 1998. The observed increase in biotechnological R&D partnerships to more than 140 newly established agreements in 1999 could signal the beginning of another period of growth of these alliances (see figure 1). At this point, it is also important to mention that, from 1994 onwards, the number of newly established pharmaceutical biotechnology partnerships maintains a relatively large, steady share of more than 20% of the total number of partnerships.

All in all, the historical data on inter-firm R&D partnering in the pharmaceutical biotechnology industry, reveal, despite some irregularities, an overall growth pattern in the number of newly established R&D partnerships since the mid-1970s. During the final years of the 1970s, we observe a very modest growth pattern while the 1980s and particularly the 1990s show an accelerated growth trend with clear peaks in 1986 and 1996 as well as a significant drop in alliance activity in 1990. This, seemingly cyclical, growth pattern is quite identical to the pattern found for other sectors of industry (see figure 1 and also Hagedoorn and van Kranenburg, 2003, for a statistical analysis of cyclical patterns in R&D partnering).

A plausible explanation for the particular pattern in the newly established biotechnological R&D alliances, found in the CATI database, is related to the instability of capital markets in the final years of the 1980s. In the first half of the 1980s, venture capital firms invested large sums of money in resource-intensive R&D projects undertaken by small, newly founded biotechnological companies (Hakansson, Kjellberg, and Lundgren, 1993; Senker, 1996; Walsh, Niosi, and Mustar, 1995). Originally based on academic research that led to important technological changes, most of the biotechnology firms were founded to commercially exploit promising new technologies, such as genetic engineering and cell fusion. Unable as yet to produce their own working capital, nearly all of the start-ups were highly dependent on venture capitalists as the single largest source of their funds.

After the stock market collapse of 1987, however, venture capitalists became increasingly pessimistic about the commercialization potential of biotechnology and their interest to invest in biotechnology firms began to wane (Barley et al, 1992; Galambos and Sturchio, 1998). The rapidly decreasing availability of venture capital during the second half of the 1980s caused an initial shakeout in the industry with large numbers of biotechnology companies filing for bankruptcy. The lower number of possible biotechnological research partners available to pharmaceutical companies may provide a tentative explanation for the substantial decrease in the number of newly established R&D partnerships during the last couple of years of the 1980s. It was also during these years that the main source of finance for biotechnology companies shifted from venture capital firms to pharmaceutical companies, which shows up in the growth of newly established pharmaceutical biotechnology partnerships during the 1990s (see also Barley et al, 1992; Senker and Sharp, 1997).

Besides this shift in the sources of investment capital, this recent upsurge in R&D alliances can also be explained by the rapid increase in biotechnological knowledge and the rise of a broad range of new technological areas triggered by influential, government-sponsored research programs, such as the US-based Human Genome Project. As a result of these developments, pharmaceutical companies and biotechnology firms increasingly engaged in alliances with others in order to carry out exploratory research across this broad range of technical areas and take advantage of the many commercial opportunities that were opening up in these fields.

Modes of cooperation

At this point, it is important to mention that established pharmaceutical firms and small, newly founded biotechnology companies typically cooperate on research through a specific number of organizational modes. These companies use a number of equity-based agreements,

such as research joint ventures and minority holdings, and a number of contractual modes, such as joint R&D agreements and R&D contracts. Before examining the specific trend in the employment of these different modes of collaboration over time, we first discuss each of these organizational arrangements somewhat further.

Of all types of inter-firm cooperation, joint ventures are probably the oldest and most widely studied form of partnering (Berg, Duncan, and Friedman, 1982; Hladik, 1985). In a research joint venture, two or more separate parent companies agree to conduct long-term, shared R&D within a distinct organizational entity or 'company' that is characterized by common equity ownership. Such equity-based joint ventures typically serve the purpose of substantially lowering the costs of transaction between the independent research partners. More specifically, partners to a joint venture are not very likely to behave in an opportunistic manner as this kind of behavior leads the whole venture to suffer and equity to diminish for the partners involved (Buckley and Casson, 1988). Minority holdings are another type of equity-based R&D partnerships where one research partner obtains a small interest (substantially less than 50%) in another company. These kinds of arrangements are typically coupled with technology exchange agreements, giving partners the opportunity to explore promising new technologies without allocating large amounts of resources to internal research.

Contractual modes of inter-firm R&D partnering, in particular joint R&D agreements, constitute an important alternative to equity-based forms of cooperation. An advantage of contractual partnerships over equity alliances is that the former group of partnerships provides research partners with a high degree of flexibility and enables them to switch from research in one technological field to another (Barley et al, 1992; Obleros and MacDonald, 1988). Joint R&D agreements involve the pooling of funds by two or more partners for the purpose of sharing technological know-how and setting up joint research and development programs.

Research contracts are examples of contractual partnerships that regulate R&D cooperation where one partner, typically a large firm, contracts another, usually a small, partner to develop a specific technology.

Relevant research indicates that the absolute numbers of contractual, non-equity R&D partnerships as well as their share in the total number of partnerships far exceed those of equity alliances (Hagedoorn, 2002; Hagedoorn and Narula, 1996). As mentioned before, equity alliances serve to raise interdependence amongst research partners whereas contractual partnerships are highly flexible relationships. In a number of high-tech sectors, such as information technology and pharmaceuticals, high costs of R&D and short technology cycles imply that most companies are unable to stay current with respect to the latest technological developments solely by relying on their internal research. By engaging in a portfolio of flexible, contract-based research partnerships, high-tech firms are able to monitor the development of several technologies at once while they can concentrate their internal research efforts on a few, most promising, development projects.

The particular trend for the proportion of contractual modes in all newly established pharmaceutical biotechnology R&D partnerships (see figure 2) is indicative of the high importance of contractual arrangements relative to equity-sharing partnerships, which coincides with findings presented in earlier contributions to the analysis of R&D cooperation in pharmaceutical biotechnology. During the second half of the 1970s, when a handful of established pharmaceutical firms such as Bristol-Myers, Eli Lilly, and Johnson & Johnson began to explore new developments in biotechnology, these companies also engaged in a number of research partnerships with biotechnological start-ups in order to gain access to new knowledge. As shown in figure 2, more than 80% of these R&D partnerships, formed during the late 1970s, are of the contractual type. Apart from a small drop in 1982, the 1980s as well as the 1990s witnessed a steady increase in the share of contractual arrangements from more

than 80% during most of the 1980s to over 90% during the final years of the 1990s. If we take a look at the specific pattern for the share of joint R&D agreements in all newly established partnerships (see also figure 2), it appears that during the second half of the 1970s and the first half of the 1980s, research contracts were the most popular mode of research interaction. From 1985 onwards, companies increasingly prefer joint R&D agreements over R&D contracts. This finding seems to indicate two major developments. First, it indicates the internalization of new biotechnological know-how by established pharmaceutical firms that have established their own research centers, which makes them less dependent on the research of specialized firms. Second, inter-firm R&D partnering in pharmaceutical biotechnology is more and more characterized by collaboration of research departments through joint R&D agreements where outsourcing of R&D itself has become less important.

-----Insert figure 2 about here-----

THE STRUCTURE OF INTER-FIRM R&D NETWORKS

Network evolution

In the previous section, we identified and described a number of important basic developments in biotechnological R&D partnering since the rise of biotechnology in the early 1970s. We now turn to an overview of major changes in the structure of research partnering networks over time, examining both network-level characteristics and partnering behavior at the level of individual firms.

Figures 3-7 give us a graphical representation of R&D partnerships in pharmaceutical biotechnology during the periods 1975-79, 1980-84, 1985-89, 1990-94, 1995-99, using a non-metric multidimensional scaling (MDS) technique. MDS is a data reduction procedure somewhat comparable to principal component analysis and other factor-analytical methods.

One of the main advantages of MDS is that it can usually, but not necessarily, fit an appropriate model in a two-dimensional picture. Particularly, MDS offers a scaling of similarity data into points lying in an X-dimensional space. The purpose of this method is to provide coordinates for these points in such a way that distances between pairs of points fit as closely as possible to the observed similarities. In order to facilitate interpretation, the solution is given in two dimensions, provided that the fit of the model is acceptable. A stress value indicates the goodness-of-fit of the configuration as this measures the proportion of the variance of the disparities that is accounted for by the MDS model, implying that lower values indicate a better goodness of fit (Hair, Anderson, Tatham, and Black, 1998). For all MDS solutions presented in this paper Kruskal's stress values (Kruskal and Wish, 1978) range from good, e.g. 0.034 for the period 1985-89, to very good, e.g. 0.001 for the period 1975-79.

Using our own network visualization software tool Najoyo (see Appendix II), we enhance the interpretability of these MDS pictures, first, by adding company labels to the dots, and, second, by drawing lines of different styles and thickness between pairs of firms with varying degrees of partnering intensity. Dotted lines represent one R&D partnership between companies, whereas solid lines indicate 2 or 3 partnerships. Thick solid lines indicate four or more alliances. See Appendix III for company labels.

During the period 1975-79, most of the established, large pharmaceutical companies were just beginning to explore biotechnology through a small number of research contracts with biotechnological firms. The early development phase of the new technology and the explorative behavior of incumbents clearly show up in the overall characteristics of the inter-firm network that came into existence during these years. Specifically, the MDS solution for the period 1975-79 (see figure 3) presents an extremely sparse, disconnected R&D network that involves a mere thirty companies where the vast majority of these companies are cooperating within the context of small, biotechnological research clusters. Many clusters are

organized around four or five research partners at the most. We also observe quite a few one-on-one partnerships between companies that are not part of any of these clusters, which is also illustrative of the very small number of partnerships that make up the network for this period. Also, the majority of firms are connected to one specific research partner through no more than one alliance.

-----Insert figure 3 about here-----

Turning to the next period, 1980-84, we observe a slightly different pattern (see figure 4). In the previous section, we found that inter-firm R&D partnering in biotechnology began to take off in the early 1980s and this strong growth trend clearly characterizes the increasingly dense research networks of the eighties. Specifically, the MDS plot for the first half of the 1980s shows a relatively dense research network where the multitude of lines connects virtually all the partners participating in the network, either directly or indirectly. Interestingly, the left hand side of figure 4 presents a part of the network that is somewhat dense because of the sheer number of partnerships between firms. By contrast, the right hand side of the figure shows a fairly concentrated area of the network that is dense because of large numbers of longer-term, repeated ties between pairs of companies. While the overall R&D network, which is for the most part based on research contracts, is relatively well-connected, we also observe a small number of one-on-one ties and some isolated research clusters at the top left hand side of figure 4.

-----Insert figure 4 about here-----

The total number of inter-firm R&D partnerships and, consequently, the R&D network density in the pharmaceutical biotechnology sector shows a substantial increase if one compares the period 1985-89 (see figure 5) with the previous one. During these years, common research efforts and many, newly established joint R&D agreements between established, large pharmaceutical firms and newly founded biotechnological companies resulted in a much denser, well-connected network structure where cooperation is mainly concentrated at the right hand side of figure 5. Nearly all firms in this dense research network are either directly or indirectly connected to each other: we observe only a small number of one-on-one links in the center of the network. Also, the number of firms that are connected to one specific research partner through at least two R&D alliances has increased, which is illustrative for the increase of the total number of R&D partnerships during the second half of the 1980s.

-----Insert figure 5 about here-----

Although figure 1 demonstrates a substantial drop in the formation of pharmaceutical biotechnology R&D partnerships in the first years of the 1990s, the MDS solution for the period 1990-94 (see figure 6) shows a fairly dense, highly connected research network where more than 300 firms have engaged in a multitude of joint R&D agreements. Particularly the top of figure 6 illustrates a very dense part of the particular network that was in existence during the first half of the 1990s. While the majority of companies making up the network for this period are connected to most other firms through their many partnerships, we also observe an isolated R&D cluster at the right hand side of figure 6. This small group of firms, consisting mainly of Chinese companies, is conducting joint biotechnological research at an isolated network position that seems completely disconnected from knowledge generated

outside this small cluster. Furthermore, throughout the network we observe a relatively large number of unique pairs of companies that are cooperating amongst themselves, but are not linked to any of the other network participants. With the exception of a small number of star players (also showing up in table 1) that have entered into multiple R&D partnerships with one single research partner, figure 6 shows relatively few solid lines.

-----Insert figure 6 about here-----

In correspondence with the large numbers of newly established R&D partnerships during the second half of the 1990s (see figure 1), the MDS plot in figure 7 shows a very large, extremely dense R&D network involving around 600 research partners that are nearly all connected to each other by the numerous direct and indirect ties. The research network is particularly concentrated at the right hand side of the figure where a small number of star players form the center of dense research clusters that are characterized by a large number of participating companies and quite a few repeated, longer-term partnerships between these companies and the star player. In general, we find a fairly large number of tightly connected couples of partnering firms that have engaged in two or more common R&D partnerships during the period 1995-99. Despite this relatively high number of repeated ties and the generally high level of network connection, we also observe nearly fifty unique pairs of companies that only cooperate amongst themselves and are thus isolated from the research network and its knowledge flows.

-----Insert figure 7 about here-----

Major players

In the above, we provided insight into the structural development of pharmaceutical biotechnology R&D networks over time by examining research collaboration at the level of general networks. Besides this aggregate level, it is useful to study research networks at the level of individual firms and evaluate the importance of particular network participants for the overall structure of the networks. For a first impression of the role played by established, large pharmaceutical firms and newly founded biotechnological companies in research networks, we refer to table 1. This table lists the ten leading network participants with most R&D partnerships in the biotechnology industry during the periods 1975-79, 1980-84, 1985-89, 1990-94, and 1995-99.

-----Insert table 1 about here-----

Our understanding of the role played by established, large pharmaceutical firms and new biotechnological companies in research networks can be clearly placed within the Schumpeterian tradition. The importance of the newly founded, entrepreneurial firm as a major generator of innovations is most clearly stressed in the 'early' Schumpeter (1934). In this early work, entrepreneurial companies are small, independent firms that act as major agents of change within new industries. These entrepreneurial companies are innovators that successfully introduce new products of which the development is expected to be largely financed through external sources and not so much through internal financial resources (cash-flow).

Many elements of such Schumpeterian entrepreneurial firms are clearly present in pharmaceutical biotechnology¹. In fact both Kenney (1986) and Powell et al (1996) depict

¹ As noted by one of the referees, it is important to mention here that not all aspects of Schumpeterian theory hold when analyzing the pharmaceutical biotechnology industry. According to Schumpeter (1934) the entrance of entrepreneurial firms into an existing industry generally leads to a 'wave of creative destruction' where established companies are driven out of the industry. As new entrants to the pharmaceutical industry were facing

new biotechnological companies as an ideal type of modern entrepreneurial firms. As mentioned by Arora and Gambardella (1990), Barley et al (1992), Pisano (1991), Powell et al (1996), small, newly founded biotechnological firms are frequently financed through venture capital or loans and equity participation of established pharmaceutical companies. Originally based on university research, that led to major scientific and technological changes, nearly all of the small, biotechnology companies also started as new entrants to the pharmaceutical industry (Kenney, 1986; Pisano, 1990; Powell, 1996).

In terms of their organizational setting and their organizational culture, most of the new biotechnological companies are quite different from the ‘standard’ company that one finds in traditional industries. New biotechnological firms seem to be driven by scientific discoveries and innovative performance and not only by regular profit-seeking (Lumerman Oliver and Porter Liebeskind, 1997). Also, the ‘academic culture’ within these innovation-driven and loosely organized companies, with their informal, non-hierarchical structures, sets them apart from many other ‘traditional’ companies (Pisano, 1991; Powell, 1996).

If we look at the role of established firms in Schumpeter, we have to understand that there is also an important role for these large companies in many publications by Schumpeter. Specifically the ‘older’ Schumpeter (1942) pictures a world of ‘modern, trustified capitalism’ where large, science-based companies dominate the innovative environment and where innovation has become routinized in large research laboratories and R&D departments. It is this particular perspective on the role of large, established companies that has for a long period, during the 1950s, 1960s, and 1970s, dominated the understanding of the role of large companies as the main source of innovation (see Kamien and Schwartz, 1982; Scherer, 1984).

In the combined biotechnology and pharmaceutical industry, the role of established companies is most clearly found in the dominant role that these firms play in the more

severe difficulties, i.e. a shortage of finance and a lack of the complementary assets required to successfully commercialize biotechnology, these firms did not replace the important role played by established pharmaceutical companies.

traditional pharmaceutical sub-sectors (Arora and Gambardella, 1990). Large firms with their extensive R&D activities and their long-term experience with time-consuming clinical trials have come to dominate the innovation process in the traditional pharmaceutical industry. This dominance is based on their leading role in incremental innovation, exploiting their current organic chemical knowledge base, and their ability to expand existing portfolios of pharmaceutical products.

Based on the literature discussed in the above, one could expect that the central role of small, newly founded biotechnology firms in research networks, as stressed in the early work of Schumpeter, is likely to be most obvious during the 1980s when many of these new companies introduced major scientific and technological breakthroughs in the pharmaceutical industry. However, as the field of pharmaceutical biotechnology has gradually matured, entrepreneurial biotechnology companies could have become less important for inter-firm R&D partnering while established firms may have become more dominant. This more dominant role for large, science-based firms in a more routinized innovative environment is particularly stressed in the later writings of Schumpeter. In the following, we will see to what extent new firms and/or established companies play an important role in research networks in the pharmaceutical biotechnology industry.

During the early years, from 1975-79, the listing of top ten R&D partnering companies holds mostly large, established pharmaceutical and chemical companies such as Ciba-Geigy, Sandoz, Johnson & Johnson, and Bayer. Only the US-based firms Genentech and Genex are small, newly founded biotechnological companies of some importance, in terms of their participation in these partnerships (see table 1). The research network for this period (see figure 3) shows a number of isolated research clusters mostly centered around the large, established pharmaceutical firms that we find in the first column of table 1. Particularly, there

are five multiple partner clusters and five dyadic partnerships, involving mostly these large firms.

During the period 1980-84, the number of large, established pharmaceutical firms and chemical companies in the top ranking, such as Johnson & Johnson and Ciba-Geigy, has decreased substantially (see table 1). During these years, the top of the list covers mainly small, newly founded, biotechnological companies, such as Genentech, Biogen, Genex, and Amgen, all from the USA. For the most part, these biotechnological companies play an important 'bridging' role in the sense that they form crucial links between networks surrounding pharmaceutical firms that otherwise would not be connected. Some clear examples of this important 'bridging' function are: Genex acts as a 'bridge' between a number of large companies, such as Bristol Myers and Pharmacia, and the large firms that are part of the network around Genentech, i.e. Roche and Baxter-Travenol Labs; Amgen serves as an important 'bridge' between the Genentech network and large companies, such as Johnson & Johnson and Abbott Labs. Apart from the increased overall density, there is another interesting aspect of the network plot for this period, found in the dense cluster around Genentech at the right hand side of figure 4 that is characterized by many repeated ties. In general, the overall network shows a fairly large number of these multi-partner clusters, with relatively few isolated partnerships.

The patterns that we observe for the period 1980-84 become somewhat different when studying the next period, i.e. the years from 1985 to 1989. The top of the list is still headed by smaller biotechnology companies, such as US-based Chiron, Biogen, and Genentech, each having more than 10 R&D partnerships during these years (see table 1). As we observed in the previous period, these small biotechnology companies, e.g. Chiron and Biogen, serve as important connections between distant parts of the network. Biogen, for example, forms a 'bridge' between the network surrounding Merck (left hand side of the MDS plot in figure 5)

and the network around SmithKline Beckman (right hand side of the figure). If we examine figure 5 more closely, we see that the biotechnological firm Genentech is still embedded in a denser cluster structure involving quite a large number of research partners with which this company has engaged in longer-term, repeated partnerships during the second half of the 1980s. However, table 1 also signals the beginning of a new development where large, established pharmaceutical companies, such as SmithKline Beckman and Johnson & Johnson, are steadily becoming more important again. Interestingly, this finding coincides with our finding that in the second half of the 1980s there is a strong increase in the use of joint R&D agreements as opposed to research contracts. This also indicates the growing role of importance for large firms in biotechnological research and the networks conducting such research. In general, the network of inter-firm partnerships has become quite complex with a relatively large number of nodal players amidst many clusters, such as Merck, Roche, Integrated Genetics, Eastman Kodak, Sandoz, Hoechst, Ciba-Geigy, Celltech, and many other companies (see also figure 5).

The increasingly important role played by large, established pharmaceutical and chemical firms in biotechnological R&D networks becomes even more obvious when we examine the list of most intensely cooperating companies for the period 1990-94 (see table 1). Most of the established companies showing up in this listing, i.e. Ciba-Geigy, Merck, Glaxo, Eli Lilly, SmithKline Beecham, and American Home Products, have formed at least 10 R&D partnerships with pharmaceutical biotechnology partners during the period 1990-94. Furthermore, their increasing importance becomes clear when looking at the R&D network in figure 6 where a number of these companies, such as Ciba-Geigy and Merck, have become star network players that are embedded in dense local research clusters with many participating partners and numerous longer-term, repeated ties. Also, most of these important network players are now directly connected to the research networks of other large players

and do not rely so much anymore on small firms fulfilling important 'bridging' roles. Ciba-Geigy, for example, is directly linked to the dense networks around a number of large companies, such as Pfizer and SmithKline Beecham. In contrast to our finding in the previous period that a small number of biotechnological research firms still held strong positions in the rank order of leading network participants, this group of companies no longer plays a role of importance during the current period. Chiron, now a medium-sized biotechnological firm and one of the few companies that has succeeded in marketing new, biotechnological drugs, obviously forms the exception (see also table 1). Being the only biotechnological firm in the listing of nodal players, this company, with its 13 R&D partnerships, holds an important position in the research network that was in existence during the period 1990-94.

For the final years of our period of analysis (1995-99), table 1 shows a list of the most central network players that only covers a number of well-known, established pharmaceutical companies, such as Roche, SmithKline Beecham, and Pfizer, and a group of more chemically oriented firms that also have some business in pharmaceuticals, such as Rhône-Poulenc, Hoechst, and Bayer. In congruence with the very dense network structure visualized in figure 7, these companies have entered into very large numbers of joint R&D agreements during the second half of the 1990s. The Roche group, which is based in Switzerland, for example, has formed a large number of 41 R&D partnerships during this period (see also table 1). The top right hand side of figure 7 shows that Roche is one of the star players we referred to previously as being embedded in a very dense local network cluster where many cluster members are connected to Roche through more than one tie. If we take a closer look at figure 7, we observe that the majority of these star players located at the right hand side of the figure are amongst the large, established firms found in the last column of table 1, such as SmithKline Beecham, Pfizer, Bristol-Myers Squibb, Glaxo Wellcome, Hoechst, Bayer, AstraZeneca, Monsanto, and Novartis. Interestingly, the relatively isolated position of these

companies and their research clusters at the right hand side of figure 7 indicates that neither the star players nor their direct partners have many links to the larger part of the network located at the center of figure 7. The formation of these research clusters seems to be a characteristic of both sparse R&D networks (see figure 3) and very dense networks (see figure 7), and much less so of networks of medium density. A final interesting characteristic of the particular R&D network shown in figure 7 is that the central players embedded in the dense, isolated clusters at the right hand side of the figure, e.g. Roche and SmithKline Beecham, are directly connected to the centers of other clusters, e.g. the ones surrounding Bristol-Myers Squibb, AstraZeneca, and Hoechst. The decreasing 'bridging' function of biotechnological companies is even more apparent in this figure than it was in figure 6.

CONCLUSIONS

Our analysis of these longitudinal data clearly suggests an overall growth in the number of annually, newly established inter-firm R&D partnerships in the pharmaceutical biotechnology industry since the 1980s. The particular growth pattern, found in the data, is explained by referring to important developments in the availability of venture capital and the influence of large-scale, governmental research projects, such as the Human Genome Program. Over time, companies active in pharmaceutical biotechnology consistently prefer contractual partnerships to equity-based alliances. The growth in R&D partnerships in pharmaceutical biotechnology is primarily caused by the employment of an increasing number of research contracts and joint R&D agreements.

In congruence with 'early' Schumpeterian views, our findings are highly indicative of the significant role played by small, entrepreneurial biotechnological companies in research networks, particularly, during the 1980s when biotechnology first became relevant for the pharmaceutical industry. During that period, small entrepreneurial biotechnological

companies did not only play a crucial role in the emergence of inter-firm networks, they also formed important bridges between sub-networks surrounding large pharmaceutical companies. The 1990s, however, seem to demonstrate a decreasing importance of these small, newly founded companies in inter-firm R&D partnering if compared to the role of large, established pharmaceutical and chemical firms. Also, the role of these small companies as bridges between major sub-networks became less prominent. During these more recent years, large companies have developed into more dominant, star players with multiple partnerships while occupying a nodal position in the pharmaceutical biotechnology inter-firm R&D network. This latter development is clearly more in line with expectations regarding inter-firm networks that are inspired by the later writings of Schumpeter.

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APPENDIX I: DATA AND SAMPLE

For our analysis, we make use of data on inter-firm R&D partnerships. These data are taken from the MERIT-Cooperative Agreements and Technology Indicators (CATI) information system (see Hagedoorn, 1993). This databank contains information on nearly 10,000 cooperative agreements in various sectors, ranging from high technology sectors such as IT and biotechnology to less technology intensive sectors, such as chemicals and heavy electrical equipment. Cooperative agreements are defined as mutual interests between independent industrial partners that are not linked through majority ownership. In the CATI database, only those agreements are being recorded that involve either a technology transfer or some form of jointly undertaken R&D. Information is also collected on joint ventures in which new technology is received from at least one of the partners, or on joint ventures having some R&D program. Other types of agreements such as production and marketing alliances are not included. Agreements formed between companies and governmental or academic institutions are generally not included in the database unless they involve at least two commercial companies.

The current paper focuses on those partnerships that were established in the period 1975-99. In the CATI databank a total of 1469 global R&D agreements involving 890 biotechnological companies and pharmaceutical firms were recorded during this time frame. Our data include equity agreements, which comprise joint ventures and minority holdings, as well as non-equity alliances that consist of joint R&D agreements and R&D contracts. The data excludes agreements that are established within the context of national and international, government sponsored, R&D cost-sharing programs. For our purpose, the most relevant information for each partnership is the number of companies involved, their names as well as the year in which the agreement was established.

APPENDIX II: NAJOJO

To facilitate our analysis and visualize the different research partnering networks that have come into existence during each of the five-year sub-periods examined in this paper, we make use of our own network visualization software tool Najoyo. As existing visualization software has serious difficulties in handling the kind of large-sized research networks that we study, we came up with the idea to develop the software tool Najoyo. This tool, which is capable of visualizing large, dense networks involving more than 500 companies, was ultimately created by Johan Willekens.

There are two separate input (text) files underlying the generation of networks in Najoyo: one file holding the MDS coordinates for each of the individual companies participating in the network and one file holding all unique company pairs and their numbers of research partnerships. On the basis of the first input file, Najoyo determines whether the particular network will be visualized in landscape (see for example figure 3,4,5, and 7) or portrait orientation (see figure 6). As a second step in the visualization process, the tool divides up the landscape- or portrait-oriented space in an X number of points. The firm coordinates held by the first input file are then mapped onto these points and visualized as dots. While creating this scatter plot, the program makes sure that the relations between dots are held constant and that dots belonging to different companies do not overlap. Thirdly, company labels are placed with the dots in such a way that they do not overlap with other labels or dots. Najoyo variably determines the font size of company labels depending on network density and the number of companies participating in the network.

Fourthly, on the basis of the second input file, Najoyo visualizes the total number of research partnerships entered into by all unique company pairs making up the network. The tool first identifies both research partners, i.e. the beginning and ending dots, and subsequently draws polybezier lines between these dots, making sure that these lines do not

cross dots belonging to companies that are not part of the partnership. The type of line (dotted, solid, and thick solid) that is drawn for each alliance intensity can be determined by the user.

APPENDIX III: LISTING OF NETWORK PARTICIPANTS

Company label	Company name
3-DP	3 Dimensional Pharmaceuticals
3M	Minnesota Mining and Manufacturing
ABBOTT	Abbott Laboratories
ABGENIX	Abgenix
ABS	American Biogenetic Sciences
ACACIA-B	Acacia Biosciences
ACADIA-P	Acadia Pharmaceuticals
ACLARAB	Aclara Biosciences
ACTIVE-B	Active Biotech
ADVANCED	Advanced Therapies
ADV-BIOT	Advanced Biotechnologies
ADV-TS	Advanced Tissue Sciences
AFFINITY	Affinity Chromatography
AFFYMAX	Affymax
AFFYMET	Affymetrix
AGA	AGA
AGOURON	Agouron Pharmaceuticals
AGRICRDC	Agricultural R&D
AG-TEC	Ag-Tec
AJINOMOT	Ajinomoto
AKZO	Akzo
AKZO-N	Akzo Nobel Nederland
ALANEX	Alanex
ALBANY-M	Albany Molecular Research
ALEXIONP	Alexion Pharmaceuticals
ALGENE	Algene Biotechnologies
ALIZYME	Alizyme
ALKERMES	Alkermes
ALKO	Alko
ALLELIX	Allelix Biopharmaceuticals
ALLERGAN	Allergan
ALLIED	Allied
ALLIED-S	Allied-Signal
ALL-PHAR	Alliance Pharmaceutical
ALTAREX	Altarex
ALTEON	Alteon
ALTHEXIS	Althexis
ALUS-LON	Alusuisse-Lonza
ALUSUISS	Swiss Aluminum
ALZA	Alza
AMBI	Ambi
AMBIONUC	American Bionuclear
AMCYAN	American Cyanamid
AMERSHAM	Amersham
AMGEN	Amgen
AMHOMEPR	American Home Products

AMRAD	Amrad
AMYLIN	Amylin Pharmaceuticals
ANERGEN	Anergen
ANESTA	Anesta
ANHEUSER	Anheuser-Busch
ANTICAN	Anticancer
APAX-P	Apax Partners
APHTON	Aphton
APOLLOB	Apollo Biopharmaceuticals
APOLLO-G	Apollo Genetics
APOLLON	Apollon Invest
APOTEX	Apotex
APP-AI	Applied Analytical
APPIMMUN	Applied Immunosciences
APR	Applied Pharma Research
APV	APV
ARADIGM	Aradigm
ARES-SER	Ares-Serono
ARGONEX	Argonex
ARIAD-P	Ariad Pharmaceuticals
ARQULE	Arqule
ARRIS-P	Arris Pharmaceuticals
ASAHI-CH	Asahi Chemical
ASTRA	Astra
ASTRA-M	Astra Merck
ASTRAZEN	Astrazeneca
ATHENA	Athena Neurosciences
ATIII	ATIII
AURORA	Aurora Biosciences
AUTOIMMU	Autoimmune
AVIAN-F	Avian Farms
AVI-BIO	AVI Biopharma
AVIRON	Aviron
AXIS-G	Axis Genetics
AXYS-AT	Axys Advanced Technologies
AXYS-P	Axys Pharmaceuticals
BAKER-CU	Baker Cummins Pharmaceuticals
BALANCEP	Balance Pharmaceuticals
BASF	Basf
BATELLE	Batelle Memorial Institute
BAUSCH&L	Bausch and Lomb
BAXTER	Baxter
BAXTER-H	Baxter Healthcare
BAXTER-T	Baxter-Travenol Laboratories
BAYER	Bayer
BECKM-C	Beckman Coulter
BECTON-D	Becton Dickinson
BEECHAM	Beecham

BERTAREL	Bertarelli
BETH-IMC	Beth Israel Medical Center
BIOCHEM	Biochem Pharma
BIOCINE	Biocine
BIOCOM	Biocom
BIOCOMPA	Biocompatibles
BIOCON	Biocontrol
BIOCRYST	Biocryst
BIOCURE	Biocure
BIODOR	Biodor
BIOGAL	Biogal
BIOGEN	Biogen
BIOGENCO	Biosource Genetics
BIO-INTR	Bio-Intermediar
BIOINVST	Bioinvest
BIOJECT	Bioject Medical Technologies
BIOMATRI	Biomatrix
BIOMEDIX	KS Biomedix
BIOMERIE	Biomerieux Alliance
BIOMET	Biomet
BIOMIRA	Biomira
BIOMOL-R	Biomolecular Research Institute
BIONEBRA	Bionebraska
BIONICHE	Bioniche
BIONUM	Bionumerik Pharmaceuticals
BIOPHARM	Biopharm
BIOPREDI	Biopredic
BIORAD	Bio-Rad Laboratories
BIORES	Biores
BIO-RESP	Bio-Response
BIOSCENE	Bioscene
BIOS-I	Biosearch Italia
BIOSIT	Biosite Diagnostics
BIOSPECT	Biospecific Technologies
BIOSYM	Biosym Technologies
BIOSYS	Biosys
BIOTA	Biota
BIOTECHN	BioTechnica
BIOTECRL	Biotech Research Laboratories
BIOThERA	Biotherapeutics
BIOTRANS	Biotransplant
BIOVECTO	Biovector Therapeutics
BNL	Brookhaven National Laboratory
BOCGROUP	British Oxygen
BOEH-MAN	Boehringer Mannheim
BOEHRI-S	Boehringer Sohn
BOHR-ING	Böhringer-Ingelheim
BORON	Boron Biologicals

BOSTONBI	Boston Biomedica
BOSTON-L	Boston Life Sciences
BRAUN-M	Braun Melsungen
BRBIO-T	British Biotech
BRBOOTS	Boots
BRIST-MS	Bristol-Myers Squibb
BRIST-MY	Bristol-Myers
BTG	BTG
BV-LABS	Ben Venue Laboratories
CADUS	Cadus Pharmaceuticals
CALBIO	California Biotechnology
CALYPTE	Calypte Biomedical
CAMB-DD	Cambridge Drug Discovery
CAMBIOSC	Cambridge Bioscience
CAMBREX	Cambrex
CAM-NS	Cambridge Neuroscience
CAMR	Camr
CAMS	Chinese Academy of Medical Sciences
CANJI	Canji
CANTAB	Cantab Pharmaceuticals
CARDICAN	Cardican
CARDO	Cardo
CARGILL	Cargill
CAT	Cambridge Antibody Technology
CATALYTIC	Catalytica
CATHAY	Cathay Clements
CATO	Cato
CCBR	CCBR
CEBTEC	Centr de Biotechnologia Agricola
CELGENE	Celgene
CELIAS	Celias
CELLCO	Cellco
CELL-G	Cell Genesys
CELLOMIC	Cellomics
CELL-PAT	Cell Pathways
CELL-T	Cell Therapeutic
CELLTECH	Celltech
CELSIS	Celsis
CELTRIX	Celtrix Pharmaceuticals
CENTAUR	Centaur Pharmaceuticals
CENTOCOR	Centocor
CEPHALON	Cephalon
CETUS	Cetus
CFVD	Centre for Vaccine Development
CHEMG-P	Chemgenics Pharmaceuticals
CH-EVER	China Everbright
CHIATAI	Chiatai Pharmaceutical Products
CHIRON	Chiron

CHIROSCI	Chiroscience
CHROMAGE	Chromagen
CHROMAX	Chromaxome
CHRYSA-I	Chrysalis
CHUGAI	Chugai Pharmaceuticals
CIBACORN	Ciba-Corning Diagnostics
CIBA-G	Ciba-Geigy
CISTRON	Cistron Biotechnology
CITIC	CITIC Technology of Beijing
CITICORP	Citicorp
CLAL-PH	Clal Pharmaceutical
CLEAR-SB	Clear Solutions Biotech
CLINIC-S	Clinical Sciences
CLONTECH	Clontech Laboratories
CNTS	CNTS
COCENSYS	Cocensys
COGNETIX	Cognetix
COLLAGEN	Collaborative Genetics
COLLARES	Collaborative Research
COLLAT-T	Collateral Therapeutics
COMBICHE	Combichem
COMGENEX	Comgenex
COMPUCYT	Compucyte
CONNAUGH	Connaught Biosciences
COOPER-I	Cooper
COPER-GS	Copernicus Gene Systems
CORANGE	Corange
CORIXA	Corixa
CORNING	Corning Glass Works
CORTECH	Cortech
CORTEX	Cortex
CORTEX-P	Cortex Pharmaceuticals
COR-THER	Cor Therapeutics
CORVAS-I	Corvas
COURTAUL	Courtaulds
CRAS	Conseils Rech. et Appl. Scientifique
CREATBIO	Creative Biomolecules
CSHL	Cold Spring Harbor Laboratory
CSL	CSL
CTA	Clinical Technologies
CUBIST-P	Cubist Pharmaceuticals
CURAGEN	Curagen
CV-THER	CV Therapeutics
CYGNUS	Cygnus Therapeutic Systems
CYTEL	Cytel
CYTO	Cyto Therapeutics
CYTOCHRO	Cytochroma
CYTOCLON	Cytoclonal Pharmaceuticals

CYTOGEN	Cytogen
CYTOMED	Cytomed
DADE	Dade
DAEWOO	Daewoo
DAINIPIC	Dainippon Ink and Chemicals
DAINIPPH	Dainippon Pharmaceuticals
DAI-PHAR	Dai-Ichi Pharmaceuticals
DAMON-B	Damon Biotech
DARWIN-M	Darwin Molecular
DEBAR	Debar
DECODE-G	Decode Genetics
DEGUSSA	Degussa
DELSYS-P	Delsys Pharmaceuticals
DELTA-W	Delta West
DEPOTECH	Depotech
DESMOS	Desmos
DEXTRA-L	Dextra Laboratories
DIADEXUS	Diadexus
DIAGBIOT	Diagnostic Biotechnology
DIAGNON	Diagnon
DIAGPROD	Diagnostic Products
DIGENE	Digene
DIGI-GT	Digital Gene Technologies
DIVERSA	Diversa
DKB	Dai-Ichi Kangyo Bank
DOW	Dow Chemical
DR REDDY	Dr Reddy Research Foundation
DRUG-RC	Drug Royalty
DSM	DSM
DUPONT	Du Pont de Nemours
DUP-PHAR	Dupont Pharmaceuticals
DURA-PH	Dura Pharmaceuticals
DYAX	Dyax
ECOGEN	Ecogen
EDB	Economic Development Board
EDITEK	Editek
EG&G-FIN	EG&G
EISAI	Eisai
ELANCORP	Elan
ELF-AQUI	Elf Aquitaine
ELILILLY	Eli Lilly
ELITE	Elite Laboratories
ELITRA	Elitra Pharmaceuticals
E-MERCK	Merck Ohg, E.
EMISPHER	Emisphere Technologies
ENDOCON	Endocon
ENDOCYTE	Endocyte
ENDOREX	Endorex

ENDOTRON	Endotronics
ENGENICS	Engenics
ENI	Ente Nazionale Idrocarburi
ENZO-BIO	Enzo Biochem
ENZON	Enzon
ENZYTECH	Enzytech
EON-LABS	Eon Laboratories
EOS-BIO	Eos Biotechnology
EPITOPE	Epitope
EPTTCO	Epttco
EQUINE	Equine Foundation
ESCA	Esca
ESTEE-L	Estee Lauder
ETH-HOLD	Ethical Holdings
EUKARION	Eukarion
EURO-DIA	Euro-Diagnostics
EUROGENT	Eurogenetics
EUR-VL	European Veterinary Laboratories
EVOTEC	Evotec Biosystems
EXELIXIS	Exelixis Pharmaceuticals
EXOCELL	Exocell
FARM	Farm
FEALQ	Fundacao de estudos Agrarios Luiz
FERMENTA	Fermenta
FIBROGEN	Fibrogen
FIMEI	Finanz. Ind. Mobiliare Ed Immob.
FLAN-HTI	Flanders High Tech Investment
FLOW-GEN	Flow General
FMC CORP	FMC
FOCAL	Focal
FOURNIER	Fournier Industrie et Sante
FRANKGEN	Frankgen
FRESENIU	Fresenius
FUISZTEC	Fuisz Technologies
FUJI-HI	Fuji Heavy Industries
FUJISAWA	Fujisawa Pharmaceuticals
FUJIZOKI	Fujizoki Pharmaceuticals
FUYO	Fuyo
GACEL	Gacel
GALAGEN	Galagen
GALENCIA	Galencia Pharmaceuticals
GALI-GEN	Galileo Genomics
GARVAN	Garvan
GED-RICH	Gedeon Richter
GENAIS-P	Genaissance Pharmaceuticals
GENELABS	Genelabs
GENELOGI	Gene Logic
GENE-M	Gene Medicine

GENENTEC	Genentech
GENE-PE	Gene Pharming
GENESIS	Genesis Pharmaceuticals
GENETECH	Genetech
GENETHON	Genethon
GENET-IN	Genetics Institute
GENETRAC	Genetrace Systems
GENETR-B	Genetronics Biomedical
GENE-TS	Gene-Track Systems
GENET-SC	Genetics Systems
GENEX	Genex
GENOS-B	Genos Biosciences
GENOVO	Genovo
GENPHARM	Genpharm
GENQUEST	Genquest
GENSET	Genset
GENSIA	Gensia Pharmaceuticals
GENSIA-S	Gensia Sicor
GENTA	Genta
GEN-TG	Gen TG
GEN-THER	Genetic Therapy
GENZ-TRA	Genzyme Transgenics
GENZYME	Genzyme
GERITECH	Geritech
GERON	Geron
GESPARAL	Gesparal
GILEAD	Gilead Sciences
GIST-BRO	Gist-Brocades
GLAXO	Glaxo
GLAXO-W	Glaxo Wellcome
GLIATECH	Gliatech
GLYCODES	Glycodesign
GLYCOMED	Glycomed
GLYCOREX	Glycorex
GPC2	Genome Pharmaceuticals
GREEN-CR	Green Cross
GREENW-P	Greenwich Pharmaceuticals
GRELAN	Greland
GRN	GRN
GRUNENTH	Grünenthal
GRYPHON	Gryphon Ventures
GRYPHONS	Gryphon Sciences
GTC	Genome Therapeutics
GUIDANT	Guidant
HAEMONET	Haemonet
HANA-BIO	Hana Biologics
HAUSER	Hauser
HAYASH-B	Hayashibira Biochemical

HEALTH-I	Healthcare Investment
HELIOSYN	Heliosynthese
HEMOSOL	Hemosol
HEM-RES	HEM Research
HERCULES	Hercules
HEXAL	Hexal Pharma
HOECHST	Hoechst
HOF-ROCH	Hoffmann-La Roche
HOL-BIO	Holland Biotechnology
HOUGHTON	Houghton
H-P	Hewlett-Packard
HPI	Houghten Pharmaceuticals
HUMAN-G	Human Genome Sciences
HYAL	Hyal Pharmaceuticals
HYBRIDON	Hybridon
HYBRITEC	Hybritech
HYGENICS	Hygenics Pharmaceuticals
HYSEQ	Hyseq
IAF-BIO	IAF Biochem
IBJ	Industrial Bank of Japan
IBM	IBM
ICAGEN	Icagen
ICI	Imperial Chemical
ICN-PHAR	ICN Pharmaceuticals
ICRF	International Cancer Research Fund
ICRT	Imperial Cancer Research Technology
IDB	IDB
IDEC	IDEC Pharmaceuticals
IDUN-P	IDUN Pharmaceuticals
ID-VAC	ID Vaccine
IGF	IGF
ILLUMINA	Illumina
IMCB	Institute of Molecular and Cell Biology
IMCERA	IMCERA
IMCLONE	Imclone Systems
IMMULOGI	Immologic Pharmaceuticals
IMMUNE	Immune Response Centre for Univial
IMMUNE-R	The Immune Response Corporation
IMMUNEX	Immunex
IMMUNIC	Immunicon
IMMUNOGEN	Immunogen
IMMUNO-L	Immunology
IMMUNOM	Immunomedics
IMMUNOTE	Immunotech
IMMUSOL	Immusol
IMPD	Institute of Medical Plant Development
IMTC	IMTC
INCELL	Incell

INCENTIV	Incentive
INCYTE-P	Incyte Pharmaceuticals
INEX-P	Inex Pharmaceuticals
INFOGEN	Infogen Systems
INGENE	Ingene
INHALETS	Inhale Therapeutic Systems
INNOGEN	Innogenetics
INS-GER	Institute of Grassland and Env. Res.
INS-GR	Institute Gustave Roussy
INS-HV	Institute of Human Virology
INSITE-V	Insite Vision
INSULINM	Insulin Mimetics
INT-CL	International Clinical Laboratories
INTE-GEN	Integrated Genetics
INTEGRA	Integra Lifesciences
INTERF-S	Interferon Sciences
INTERL-2	Interleukin-2
INTERNEU	Interneuron Pharmaceuticals
INT-GENO	Integrated Genomics
INT-M&C	Int. Minerals and Chemicals
INTRABIO	Intrabiotics Pharmaceuticals
INTROGEN	Introgen Therapeutics
IOB	Institute of Botany
I-PASTEU	Institut Pasteur
ISIS	Isis
ISIS-PH	Isis Pharmaceuticals
IXSYS	Ixsys
J&J	Johnson and Johnson
JAGO	Jago Pharma
JAGOTEC	Jagotec
JOHNSHOP	Johns Hopkins Health System
JOSLIN-D	Joslin Diabetes Centre
JOUVEINA	Jouveinal
JPN-NIH	Japan NIH
JPN-TOB	Japan Tobacco
KABI	KABI Pharmacia
KAISER-B	Kaiser Biotech
KAKETSUK	Kaketsuken
KANEBO	Kanebo
KANEGAFU	Kanegafuchi Chemical
KARO-BIO	Karo Bio
KAROLINS	Karolinska Institute
KIRIN	Kirin Brewery
KISSEI-P	Kissei Pharmaceuticals
KODAK	Eastman Kodak
KOSAN-B	Kosan Biosciences
KOTO-F	Kotobuki Fudosan
KUNMING	Kunming Pharmaceutical Factory

KYOWA-HK	Kyowa Hakko Kogyo
KYOWA-MC	Kyowa Medex
LABLAFON	Laboratoire L. Lafon
LAB-SERV	Laboratoires Servier
LAB-SOPH	Laboratorios Sophia
LAJOLLA	La Jolla Pharmaceutical
LASURE	Lasure and Crawford
LBL	Lawrence Berkeley Laboratory
LEOFONDE	Leo Fondet
LEUKOSIT	Leukosite
LEX-GEN	Lexicon Genetics
LG-CHEM	LG Chemical
LIGAND	Ligand Pharmaceuticals
LILLY	Lilly
LIMAGR	Limagrain
LION-BIO	Lion Bioscience
LIONS	Lions Lyc. Institute
LIPOTECH	Liposome Technology
L'ORÉAL	L'Oréal
LRC	London Rubber
LUDWIG	Ludwig Institute for Cancer Research
LUNDB-FO	Lundbeckfonden
LXR-BIOT	LXR Biotechnology
LYNX-TH	Lynx Therapeutics
MACROCH	Macrochem
MACRONEX	Macronex
MAGAININ	Magainin Pharmaceuticals
MALLIN-G	Mallinckrodt
MARIE-CC	Marie Curie Cancer Care
MARION	Marion Laboratories
MARIO-NI	Mario Negri Institute
MARKET-B	Market Biosciences
MDL-IS	MDL Information Systems
MDS-HG	MDS Health
MDS-PANL	MDS Panlabs
MEDAC	Medac Ges. für Klinische Spezialpräparate
MEDAREX	Medarex
MEDEVA	Medeva
MEDIGENE	Medigene
MEDIMMUN	Medimmune
MED-RC	Medical Research Council
MEDTRON	Medtronic
MEGABIOS	Megabios
MEIJI-SK	Meiji Seika Kaisha
MENARINI	Menarini Industrie Farmaceutiche
MERCK	Merck
MERCK-KG	Merck Kgaa
METABOLE	Metabolex

METABOLM	Metabolic Modulators Research
METRA	Metra
MICROFAC	Micro-Facilities
MICROGEN	Microgenomics
MICROM	Micromet
MI-KASEI	Mitsubishi Kasei
MILLENPH	Millennium Pharmaceuticals
MILLIPOR	Millipore
MIMETIX	Mimetix
MIT-CHEM	Mitsubishi Chemical
MITOTIX	Mitotix
MIT-S-CHE	Mitsubishi Gas Chemical
MITSUBIS	Mitsubishi
MIT-SUI	Mitsui
MOCHIDA	Mochida Pharmaceuticals
MOLBI	Molecular Biosystems
MOL-DYN	Molecular Dynamics
MOL-GEN	Molecular Genetics
MOL-GERI	Molecular Geriatrics
MONOCLAB	Monoclonal Antibodies
MONSANTO	Monsanto
MORISHIT	Morishita Pharmaceutical
MORPHO	Morphosys
MOTOROLA	Motorola
MRC-COL	MRC Collaborative Center
MYCO-PH	Myco Pharmaceuticals
MYRIAD-G	Myriad Genetics
NANFANG	Shenzhen Nan Fang Pharmaceuticals
NANJING	Nanjing
NANOGEN	Nanogen
NANOSYST	Nanosystems
NASTECH	Nastech Pharmaceutical
NAV	North American Vaccine
NCI	NCI
NEOPATH	Neopath
NEOPROBE	Neoprobe
NEOSE-T	Neose Technologies
NESTLÉ	Nestlé
NEUGENE	Neugenesis
NEURAL-B	Neuralstem Biopharmaceuticals
NEUREX	Neurex
NEUROCH	Neurochem
NEUROCRI	Neurocrine Biosciences
NEUROG	Neurogen
NEUROGEN	Neurogena
NEUROSEA	Neurosearch
NEUROVIR	Neurovir
NEXAGEN	Nexagen

NEXSTAR	Nexstar Pharmaceuticals
NEXTRAN	Nextran
NIP-KAYA	Nippon Kayaku
NIP-SODA	Nippon Soda
NIP-SUIS	Nippon Suisan Kaisha
NISSAN	Nissan
NITROMED	Nitromed
NITTA	Nitta Gelatin
NORDISKG	Nordisk Gentoft
NORSK-HY	Norsk Hydro
NOVALON	Novalon Pharmaceuticals
NOVAPHAR	Nova Pharmaceuticals
NOVARTIS	Novartis
NOVO-IND	Novo Industri
NOVO-NOR	Novo-Nordisk
NOVOPHAR	Novopharm Biotech
NPM	Nederlandse Participatie Mij.
NPS-PHAR	NPS Pharmaceuticals
NYU	New York University
OCEAN-P	Ocean Pharmaceuticals
OCLASSON	Oclasson
OGS	Oxford Glycosystems
OMEGA	Omega
ONCOGEN	Oncogen
ONCOGENE	Oncogene Science
ONO	Ono Pharmaceuticals
ONTOGEN	Ontogen
ONTOGENY	Ontogeny
ONYX	Onyx Pharmaceuticals
OPG	OPG Apothekers Cooperatie
ORAVAX	Oravax
ORGANOGE	Organogenesis
ORGANOGN	Organogen
ORTHO-D	Ortho Diagnostics
OSI-P	Osi Pharmaceuticals
OSIRIS-T	Osiris Therapeutics
OSTBIO	Osteometer Biotech
OTSUKA	Otsuka Pharmaceuticals
OXAGEN	Oxagen
OX-BIO	Oxford Biosciences
OXF-ASY	Oxford Asymmetry
OXF-BIOM	Oxford Biomedica
OXF-GLYC	Oxford Glycosciences
OXF-MOL	Oxford Molecular
OXIGENE	Oxigene
P&U	Pharmacia and Upharm
PACK-BIO	Packard Bioscience
PACLIA	Pacific Liaisons

PACNW-RF	Pacific Northwest Research Foundation
PALOMA	Paloma Partners
PANDEX-L	Pandex Laboratories
PANLABS	Panlabs
PARA-BIO	Paradigm Biosciences
PARACEL	Paracelsian
PARAD-G	Paradigm Genetics
PARATEK	Paratek Pharmaceuticals
PARNIB	Participatiefonds NIB
PARTNERH	Partners Healthcare System
PAST-MER	Pasteur-Merieux MSD
PAZ	PAZ
PDC	Pharmaceutical Discovery
PEP-THER	Peptide Therapeutics
PEPTIDE	Peptide Technology
PEPTOR	Peptor
PERKIN-E	Perkin-Elmer
PERSEPT	Perceptive Biosystems
P-FABREP	Pierre Fabre Participations
PFIZER	Pfizer
PHARMA	Pharmagenesis
PHARMACI	Pharmacia
PHARMACO	Pharmacopeia
PHARMAG	Pharmagene Laboratories
PHARMAGE	Pharmagenics
PHARMA-P	Pharma Patch
PHARMASS	Pharmasset
PHARMAV	Pharmavene
PHARMECO	Pharm-Eco Laboratories
PHARMOS	Pharmos
PHARM-UA	Pharmacia and Upjohn
PHARPROT	Pharmaceutical Proteins
PHAR-RES	Pharmaceutical Resources
PHERIN	Pherin Pharmaceuticals
PHILLIPS	Phillips Petroleum
PHYLOS	Phylos
PHYTERA	Phytera
PHYTON	Phyton Catalytic
PHYTON-B	Phyton
PHYTOPHA	Phytopharmaceuticals
PIERREL	Pierrel
PLIVA	Pliva
PMSV	Pasteur Merieux Serums et Vaccins
POLYCELL	Polycell
POWDERJ	Powderject Pharmaceuticals
POWERCO	Power Corporation of Canada
PPL-THER	Ppl Therapeutics
PRES-PHA	President Pharmaceutical

PRIONICS	Prionics
PRIZM	Prizm
PRIZM-P	Prizm Pharmaceuticals
PROCEPT	Procept
PROCOR-N	Procordia Nova
PROCT&GA	Procter and Gamble
PROGEN	Progenics Pharmaceuticals
PROLIFIX	Prolifix
PROMEGAB	Promega Biotech
PROSCRIP	Proscrip
PROT-DL	Protein Design Laboratories
QIAGEN	Qiagen
QLT	Quadra Logic Technologies
QUADRA-H	Quadrant Healthcare
QUARK-B	Quark Biotech
QUIDEL	Quidel
R&C	Reckitt and Colman
RABO-BVF	Rabobank Biotech Venture Fund
RANBAXY	Ranbaxy Laboratories
RECORDAT	Recordati Industria Chimica E Farmaceutica
REGENER	Regeneron Pharmaceuticals
REGNERI	Regneri Unternehmen
RENT-ARZ	Rentschler Arzneimittel
REPLIGEN	Repligen
RESOLUT	Resolution Pharmaceutical
RESSI	Ressi
RETROP-S	Retroperfusion Systems
REVLON	Revlon
RGENE	R Gene Therapeutics
RHONE-P	Rhône-Poulenc
RIBOGENE	Ribogene
RIBOZYME	Ribozyme Pharmaceuticals
RIGEL	Rigel
ROBERTS	Roberts Pharmaceuticals
ROCHE	Roche
ROHM&HS	Rohm and Haas
ROSWELLP	Roswell Park Cancer Institute
RP-SCHER	RP Scherer
RTI	Research Triangle Institute
RTZ	Rio Tinto-Zinc
SAGAMI	Sagami Chemical Research
SANDOZ	Sandoz
SANDOZ-P	Sandoz Pharma
SANG-A	Sang-A
SANGSTAT	Sangstat Medical
SANKYO	Sankyo
SANO	Sano
SANOFI	Sanofi

SANWA	Sanwa
SANWA-KK	Sanwa Kagaku Kenkyusho
SBMP	Snow Brand Milk Products
SCHEIN-P	Schein Pharmaceutical
SCHERER	Scherer
SCHERERH	Scherer Healthcare
SCHERING	Schering
SCH-PLOU	Schering-Plough
SCHWAR-M	Schwar-Mann
SCHWARZ	Schwarz Pharma
SCIOS	Scios
SCIOS-N	Scios Nova
SCOTGEN	Scotgen
SCOTIA	Scotia Pharmaceuticals
SCOTIA-H	Scotia
SCRIPGEN	Scripgen
SCRIPTGE	Scriptgen Pharmaceuticals
SEARLE	Searle
SEIKAGAK	Seikagaku Kogyo
SENSUS	Sensus Technologies
SEPRACOR	Sepracor
SEQUA	Sequa
SEQUANA	Sequana Therapeutics
SEQUUS	Sequus Pharmaceuticals
SERAGEN	Seragen
SERVI	Servier Laboratoires
SHAMAN	Shaman Pharmaceuticals
SHEF-P	Sheffield Pharmaceuticals
SHELL	Shell
SHIELD	Shield Diagnostics
SHIONOGI	Shionogi
SIB/IA	Salk Institute Biotechnology
SIBA-S	Siba Self Medication
SIBIA	Sibia
SIBIA-N	Sibia Neurosciences
SIGA-P	Siga Pharmaceuticals
SIGMA-T	Sigma-Tau
SIGNAL-P	Signal Pharmaceuticals
SINO-GEN	Sino Genetic
SLOAN	Sloan Kettering Institute
SMALL-MT	Small Molecule Therapeutics
SMITH&N	Smith and Nephew
SMKB	Smithkline Beckman
SMKBEECH	Smithkline Beecham
SOC-SGF	Societe Generale de Financement du Quebec
S-OIL-IN	Standard Oil of Indiana
SOLVAY	Solvay
SOMATIX	Somatix

SOMATOGN	Somatogenetics
SONUS-P	Sonus Pharmaceuticals
SPECTRAB	Spectra Biomedicals
SPHERE-B	Sphere Biosystems
SPHINX-P	Sphinx Pharmaceuticals
SQUIBB	Squibb
SRI	SRI
SRYKER	Sryker
SS-PHARM	SS Pharmaceuticals
STATE-TR	State Trustees
STEM-CS	Stem Cell Sciences
STERITEC	Steritech
STERLING	Sterling Drug
STRATA-B	Strata Biosciences
STRESSGE	Stressgen Biotechnologies
STRUCT-B	Structural Bioinformatics
STRYKER	Stryker
SUGEN	Sugen
SULZER	Sulzer
SUMIT-CH	Sumitomo Chemical
SUMITOMO	Sumitomo
SUMIT-RU	Sumitomo Rubber
SUNTORY	Suntory
SUPER-G	Supergen
SUPRAGEN	Supragen
SURVIVAL	Survival Technology
SUZ-PH	Suz Pharma
SWEDBACL	Swedish Bacteriological Laboratories
SYMBOLL	Symbollon
SYMPHAR	Symphar
SYNAPTIC	Synaptic Pharmaceutical
SYNBIOT	Synbiotics
SYNERGEN	Synergen
SYNSORB	Synsorb Biotech
SYNTEM	Syntem
SYNTEX	Syntex
SYNTRO	Syntro
TAIHO	Taiho Pharmaceuticals
TAIHO-A	Taiho Alberta
TAISHO	Taisho Pharmaceuticals
TAKARA	Takara Shuzo
TAKEDA	Takeda Chemical
TANABE	Tanabe Seiyaku
TANG-FR	Tang Freres
TANOX	Tanox Biosystems
TAP	TAP
TARGACEP	Targacept
TARGET-G	Targeted Genetics

TBC	Texas Biotechnology
T-CELL-S	T Cell Sciences
TECHNICL	Techniclone
TEIJIN	Teijin
TELIK	Telik
TELIOS-P	Telios Pharmaceuticals
TERRAGEN	Terragen Discovery
TERRAPIN	Terrapin Technologies
THERA-A	Therapeutic Antibodies
THERAGEN	Theragen
THERATEC	Theratech
THEREXS	Therexsys
THERION	Therion Biologics
THLIPOCO	The Liposome Company
THROMBO	Thrombosys
TKT	Transkaryotic Therapies
TNO	TNO
TOWER-PH	Towers Phytochemical
TOYOBO	Toyo Boseki
TOYOSODA	Toyo Soda
TRACE	Trace Computers
TRANSGEN	Transgène
TREDEGAR	Tredegar Industries
TREGA-B	Trega Biosciences
TRINITY	Trinity Biotech
TRIPOS	Tripos
TROPIXP	Tropix Pharmaceuticals
TSUMURA	Tsumura Juntendo
TUDOR-IG	Tudor Investment
TULARIK	Tularik
UCB	Union Chimique Belge
U-GENER	U-Gene Research
UNC	UNC
UNIVAX	Univax Biologics
UN-TECHN	United Technologies
UPJOHN	Upjohn
UROGEN	Urogen
US-BIOMA	US Biomaterials
USINE23	Usine 23
VANGUARD	Vanguard Medica
VECTORPH	Vectorpharma
VERTEX	Vertex Pharmaceuticals
VESTAR	Vestar
VIAGENE	Viagene
VICAL	Vical
VIMRX-P	Vimrx Pharmaceuticals
VINELAND	Vineland Laboratories
VION-P	Vion Pharmaceuticals

VIRAL-T	Viral Therapeutics
VIROGEN	Virogenetics
VIROPHAR	Viropharma
VIRUS-RI	Virus Research Institute
VOLVO	Volvo
VYREX	Vyrex
WADLEY	Wadley Technologies
WARNER-L	Warner-Lambert
WELLCOME	Wellcome
WEYERH	Weyerhauser
WRGRACE	W.R. Grace
WUXI	Wuxi Pharmaceuticals
WYETH-R	Wyeth-Ayerst Research
XECHEM	Xechem
XENOMETR	Xenomatrix
XENOVA	Xenova
XOMA	Xoma
XTL-BIO	XTL Biopharmaceuticals
YAMANOU	Yamanouchi Pharmaceuticals
YOSHITOM	Yoshitomo Pharmaceutical
ZAMBON	Zambon
ZELTIA	Zeltia
ZENECA	Zeneca
ZENYAKU	Zenyaku Kogyo
ZTB	ZTB
ZYCOS	Zycos
ZYMOGEN	Zymogenetics
ZYNAXIS	Zynaxis

Figure 1. Growth of numbers of newly established R&D partnerships in general and in pharmaceutical biotechnology, 1975-99; *source*: MERIT-CATI.

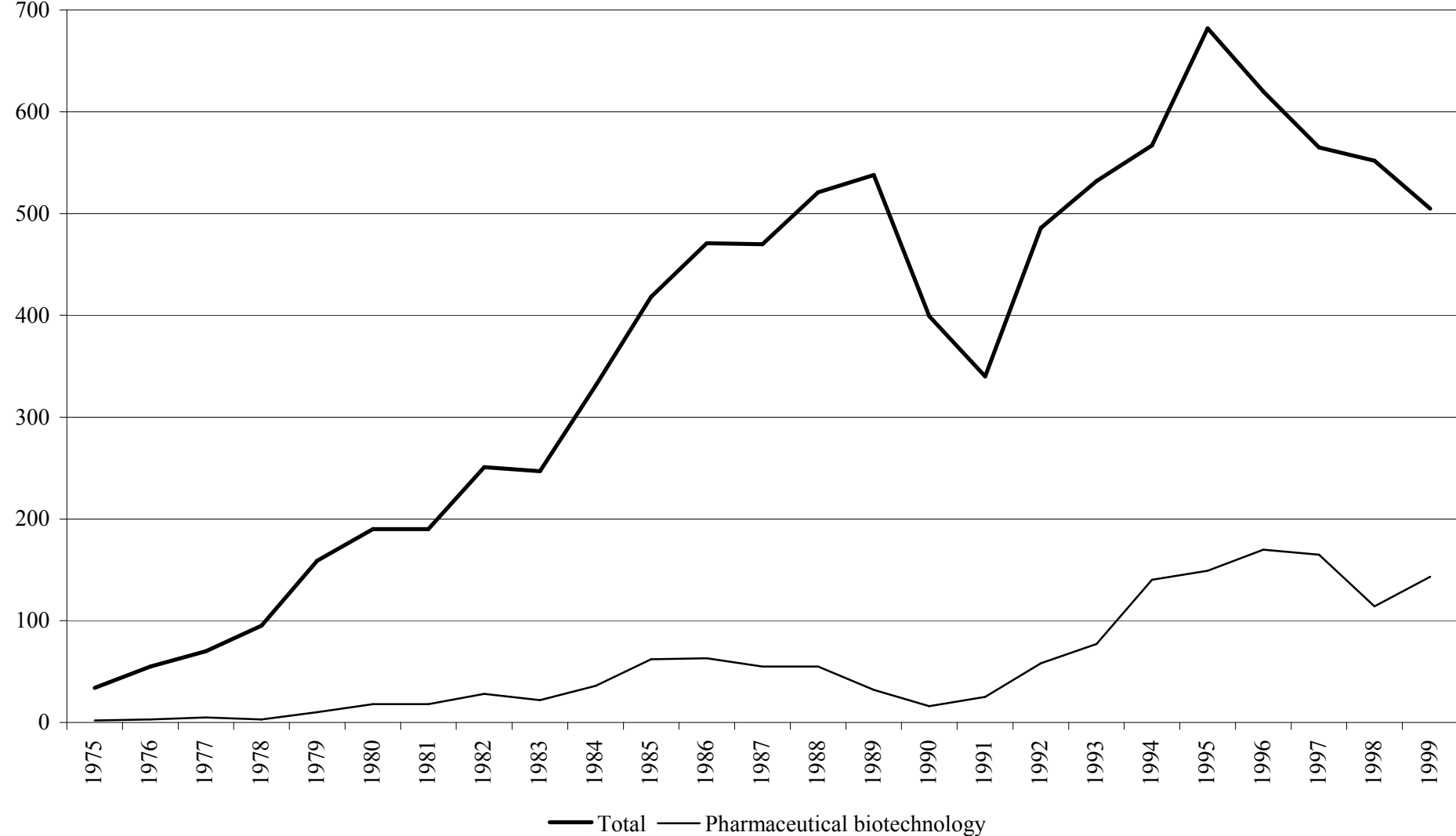


Figure 2. The share (%) of all contractual modes and joint R&D agreements in all newly established pharmaceutical biotechnology R&D partnerships, three year moving averages, 1975-99; *source*: MERIT-CATI.



Table 1. A comparison of the top ten firms with the most R&D partnerships in pharmaceutical biotechnology in 1975-79, 80-84, 85-89, 90-94, and 95-99 (numbers in brackets).

1975-79		1980-84		1985-89		1990-94		1995-99	
1. Ciba-Geigy	(4)	Genentech	(14)	Chiron	(12)	Ciba-Geigy	(18)	Roche	(41)
2. Marion Laboratories	(3)	Biogen	(10)	Biogen	(12)	Merck	(15)	SmithKline Beecham	(28)
3. Procordia Nova	(3)	Genetic Systems	(9)	SmithKline Beckman	(11)	Glaxo	(14)	Pfizer	(23)
4. Genentech	(3)	Genex	(8)	Eastman Kodak	(11)	Eli Lilly	(14)	Bristol-Myers Squibb	(23)
5. Genex	(2)	Johnson & Johnson	(8)	Genentech	(11)	Chiron	(13)	Rhône-Poulenc	(22)
6. Sandoz	(2)	Amgen	(6)	Johnson & Johnson	(10)	SmithKline Beecham	(13)	Glaxo Wellcome	(22)
7. Schering	(2)	Syntex	(6)	California Biotechnology	(10)	American Home Products	(10)	Eli Lilly	(19)
8. Johnson & Johnson	(1)	Mitsui	(6)	Celltech	(9)	Eastman Kodak	(8)	Hoechst	(17)
9. Bayer	(1)	Cetus	(6)	Genetics Institute	(9)	Hoechst	(8)	Bayer	(15)
10. Baxter-Travenol Laboratories	(1)	Ciba-Geigy	(5)	Du Pont de Nemours	(9)	Rhône-Poulenc	(7)	Warner-Lambert	(15)

Source: MERIT-CATI databank.

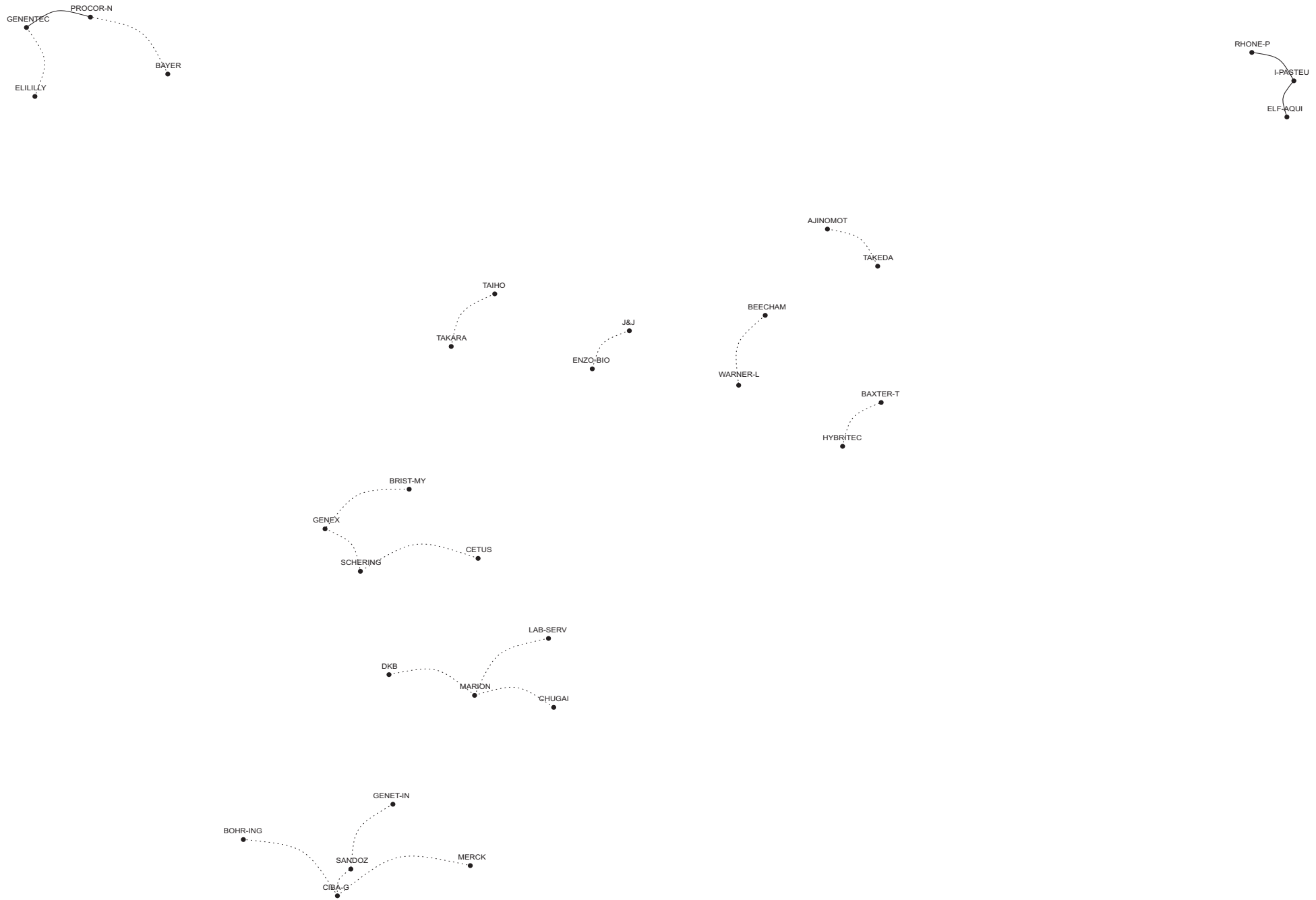


Figure 3. Inter-firm R&D partnerships amongst cooperating companies in pharmaceutical biotechnology, 1975-79; *source:* MERIT-CATI.

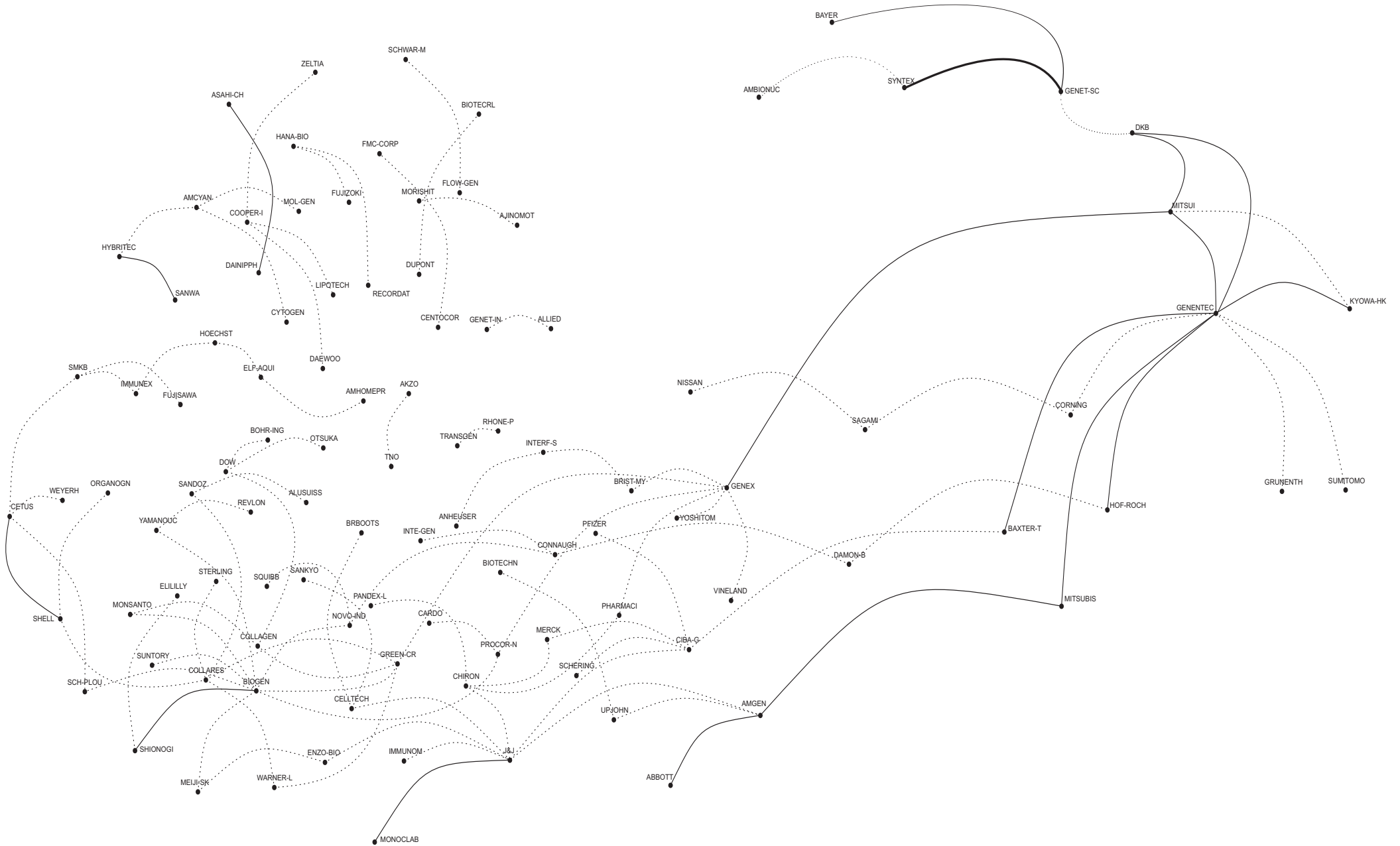


Figure 4. Inter-firm R&D partnerships amongst cooperating companies in pharmaceutical biotechnology, 1980-84; *source*: MERIT-CATI.

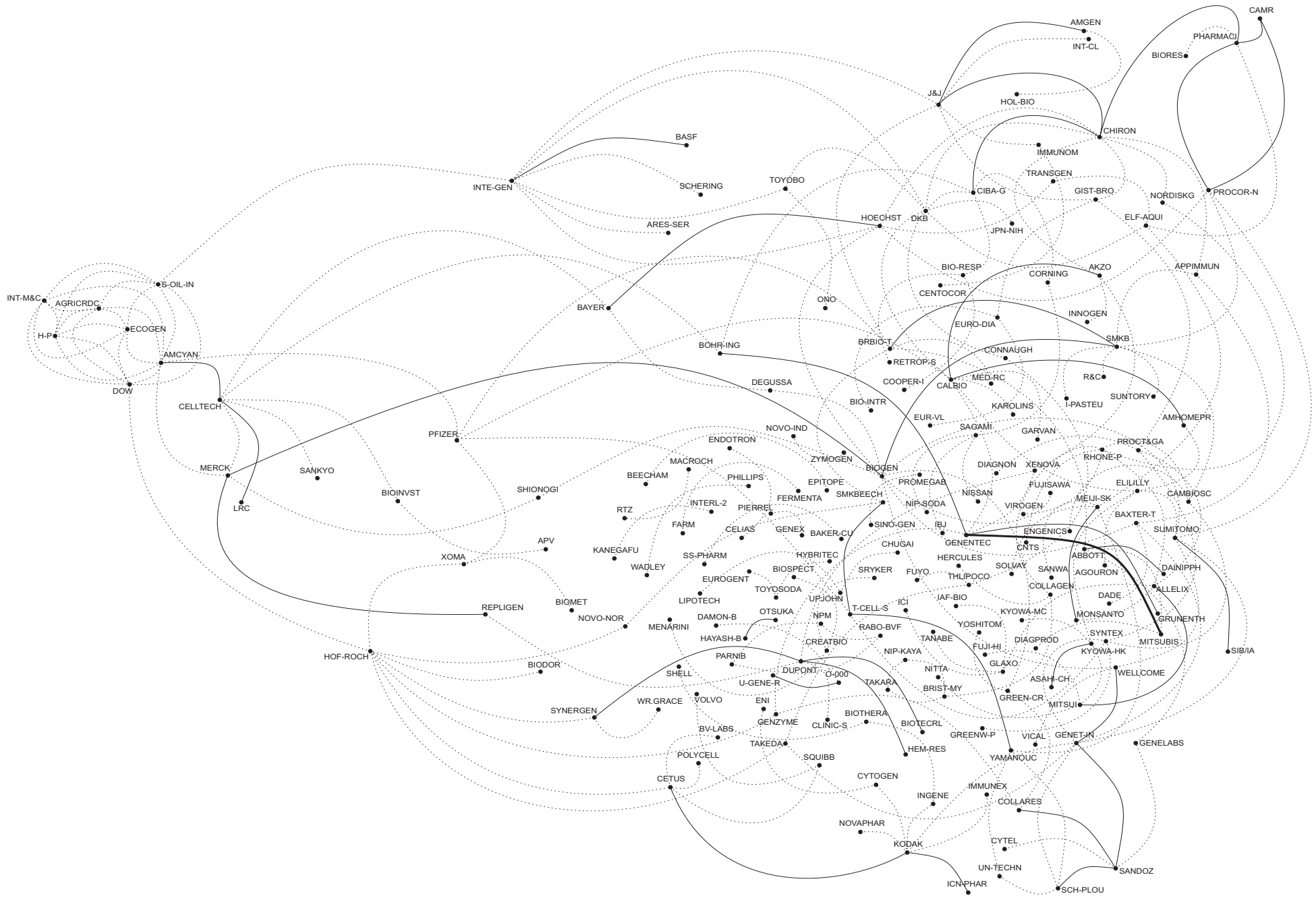


Figure 5. Inter-firm R&D partnerships amongst cooperating companies in pharmaceutical biotechnology, 1985-89; *source*: MERIT-CATI.

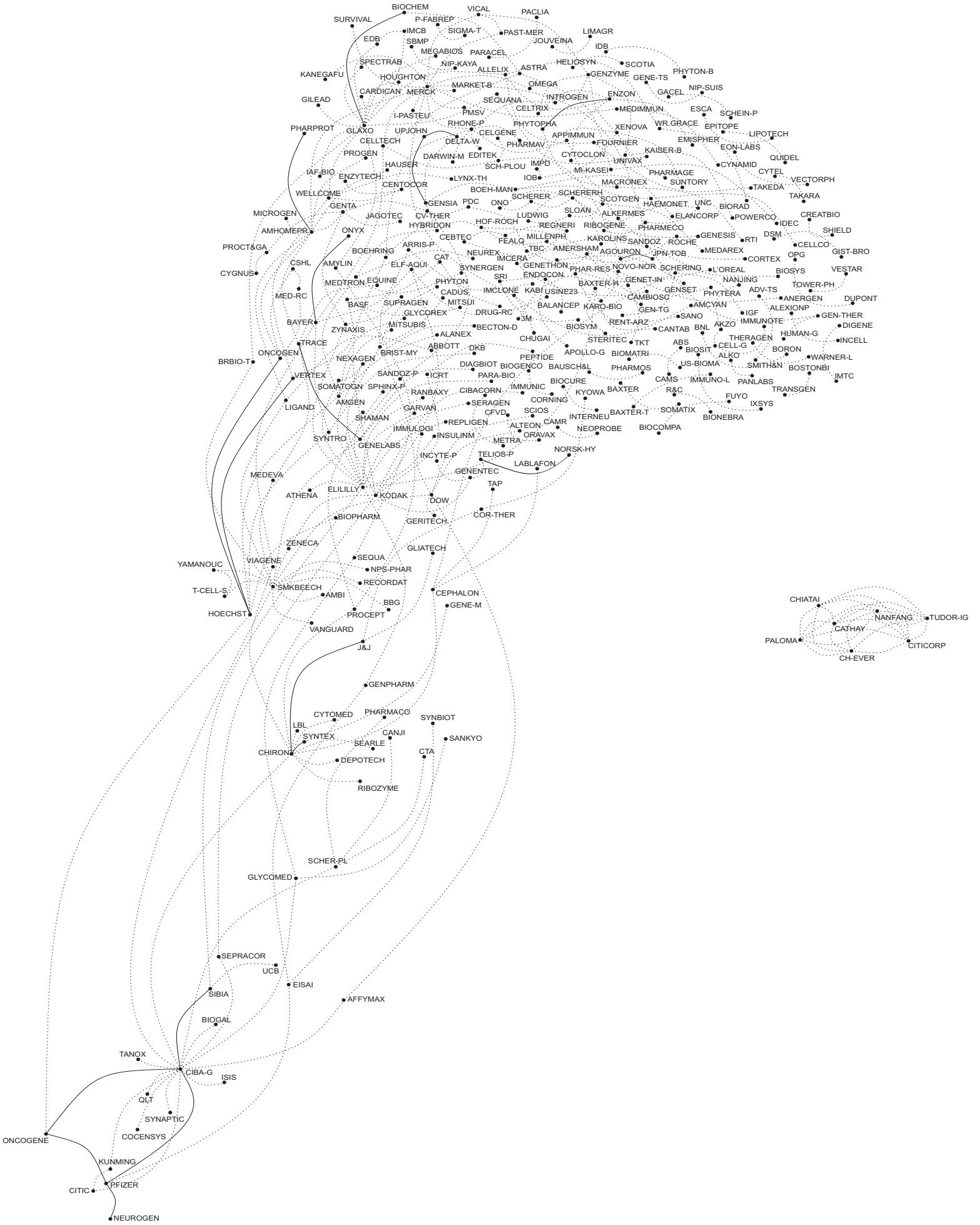


Figure 6. Inter-firm R&D partnerships amongst cooperating companies in pharmaceutical biotechnology, 1990-94;
 Source: MERIT-CATI.

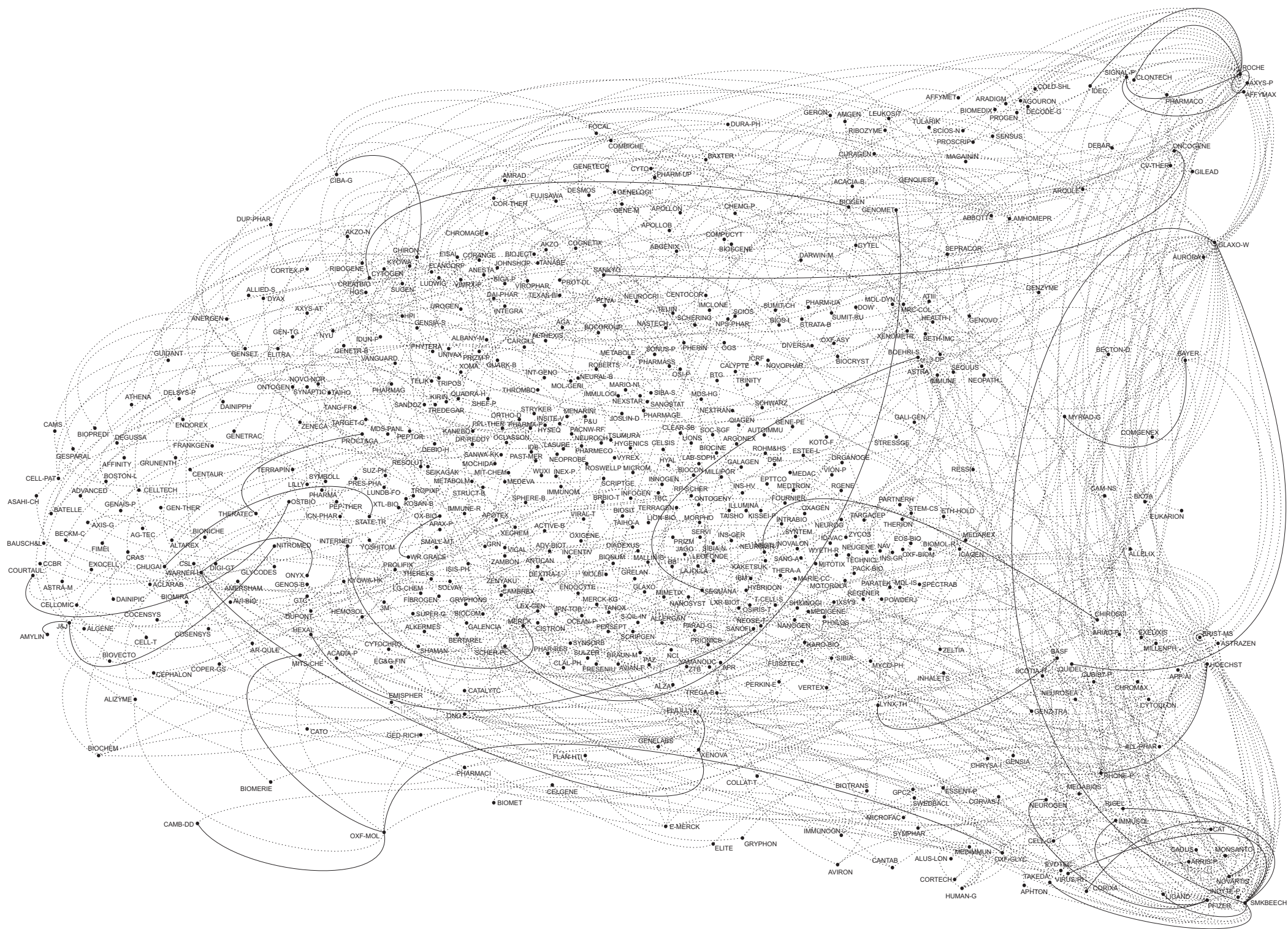


Figure 7. Inter-firm R&D partnerships amongst cooperating companies in pharmaceutical biotechnology, 1995-99; *source*: MERIT-CATI.