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Alliances are not enough explaining rapid growth in biotechnology firms

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Abstract

The goal of this paper is to understand the factors explaining differential growth in biotechnology firms. It aims also to add some caution to the generalized opinion according to which alliances are the key factor behind new firm performance. The theoretical framework is based on competence, and evolutionary theories of the firm. These approaches underline the fact that within similar industries and technologies firms display clear and persistent variety in performance. Some 60 dedicated biotechnology firms (DBFs) were interviewed across Canada; half of them experienced rapid growth. A few variables, including alliances, explained much of the fast growth.

Keywords: Biotechnology; R&D; Alliances; Performance; Canada

1. Introduction

Biotechnology is one of the three generic technologies that emerged in the postwar period, together with information technologies and advanced materials. Biotechnology has several distinctive traits that distinguish it from the two others. Most important, biotechnology has emerged from university research, and thousands of firms have been created in the last 20 years in all developed countries. Also, dedicated biotechnology firms (DBFs) have competed, and cooperated, with established pharmaceutical and chemical firms. DBFs have been the object of many important studies on the rise, growth, organization and market structure and an entirely new activity (see among others, Powell and Brantley, 1992; Powell et al., 1996; Lerner and Merges, 1997; Mytelka, 1999; Baum et al., 2000). One important constant in these studies is that alliances and cooperation appear as the key factor explaining the survival and the growth of the new biotechnology firms. Alliances convey resources and credibility to the entrepreneurial DBFs. This paper tends to balance the received view with the consideration of other key factors bringing financial resources and credit to the dedicated biotechnology firms, and contributing to their survival and growth.

2. Theory

2.1. The previous literature

Differential growth of enterprises was the central concern of Penrose (1959) in her seminal work on the theory of the growth of the firm. She postulated that

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differential growth was the result of internal resources and activities, particularly management capabilities and behavior. Later, Rumelt and others showed that the growth of firms was more a firm-specific than an industry-specific phenomenon. In other words, firm characteristics mattered more than industry fluctuations (Rumelt, 1991). Their work has founded some of the most influential currents of management thought in the last 20 years: namely, resource-based and competencies theories of the firm (Foss, 1997; Foss and Knudsen, 1996; Hamel and Heene, 1994; Hamel and Prahalad, 1994). According to these theories, firm growth is dependent on the internal management capabilities of the organization, particularly in the areas of production, R&D, finance and marketing.

Another group of theories has put the accent on external factors of growth. In biotechnology, external financing and strategic alliances have been considered key factors of growth, as they tend to overcome the chronic resource-dependence of emerging firms (Barley et al., 1992; Das and Teng, 2000; Gulati, 1998; Niosi, 1995; Powell et al., 1996; Senker, 1996).

A fluid venture capital environment, as well as the firm's ability to tap resources from that environment, is also considered a major growth factor of successful DBFs (Kenney, 1986). Biotechnology firms tend to cluster in regions where venture capital is abundant.

In the same vein, the capability to attract ideas from research universities and government laboratories is a key factor of growth in these science-based activities (Enright, 1998; Kenney, 1986; Prevezer, 1998). Firms located in regions with abundant venture capital and prolific scientific institutions are more likely to grow than those in backward regions (Powell, 1999; Zucker et al., 1998). The institutional environment seems to play an even greater role in the national system of innovation perspective: only nations with adequate research and financial systems really develop successful biotechnology firms (Bartholomew, 1997).

Internal and external growth factors are complementary. The core competencies of DBFs lie in R&D (Pisano, 1991). Large pharmaceutical, chemical and grain-trading corporations have a more varied spectrum of competencies, including in clinical trials, patenting, manufacturing and marketing. Thus, biotechnology firms prosper if they are able to create alliances with large corporations that will provide financial resources, manufacturing, marketing and regulatory expertise to the emerging DBF. Venture capital firms also provide financial abilities, but force the DBF to hire professional managers and thus diversify the core capabilities of the firm. These partners (large corporations and venture capital firms) bring external resources and competencies to the DBFs. Networks of DBFs, venture capital firms, large corporations and research institutions are key in the dynamics of biotechnology.

A less abundant literature has examined more in detail the differential growth rate of new, high-technology firms (Eisenhardt and Schoonhoven, 1990). Since the mid 1960s, authors have been aware of the liabilities of newness and smallness (Stinchcombe, 1965). Also, the literature has stressed the importance of starting conditions in these new firms. These conditions include the founding team (its quality and size) (Zucker et al., 1998), the main strategic decisions (project and product choice, markets targeted)(Cooper, 1998), and the environment (Powell, 1999). Once the initial conditions have been set, some level of structural inertia occurs. This may be particularly true in small firms such as DBFs, with limited resources and information.

Not unlike competence theories of the firm, evolutionary economics and management theory have insisted on the fact that firms start operating with very different initial configurations of factors, target niches and missions. Once the initial conditions are set, they are difficult to change (Nelson, 1995; Ryan et al., 1995). Thus, new firms having targeted agricultural biotechnology at the start will not easily move to human health activities, even if these appear to be more successful or promising. Growth, therefore, depends at least partially on the initial niches the founders have chosen for the firm and which are difficult to modify once the firm is operating. Path dependent process set up, including contracts, learning activities and others that tend to "fix" even new firms in a given trajectory (Arthur, 1994). Biotechnology is an evolutionary activity punctuated by major innovations (McKelvey, 1996).

2.2. A few major hypotheses

We can derive a few major hypotheses from the above discussion. They relate to both strategy and internal conditions of rapid growth, as well as to the

environment and external conditions. Rapid growth depends on.

H1: Targeting high-growth product niches

Biotechnology products and markets are not all born equal. The early predictions of bonanza for all markets (Kenney, 1986) have now receded in favor of a more parsimonious view of some applications of high-growth potential (mainly linked to human health and drug discovery) and others with slow growth (mainly food and agricultural biotechnology)(Wald, 1996). Bounded-rationality characterizes managers in all firms, including DBFs. Scientist-entrepreneurs in many DBFs have been slow in recognizing that some of the new biotechnology products (mainly modified plants and animals for human consumption) could eventually meet high levels of consumers' resistance. With or without alliances, the chances of success for the new DBFs in these blocked ways, are slim. This hypotheses underlines the importance of demand factors for innovation and growth to occur.

H2: Targeting major (export) markets

Knowledge-intensive products, such as those targeted by DBFs, are characterized by increasing returns to scale: they have high upfront costs (from R&D and marketing) and rapidly declining production costs per unit (Arthur, 1994; Niosi, 2000). Targeting world markets is the best way to maximize returns on a pharmaceutical product, be it a new drug, a vaccine or a diagnostic kit. Again, this second hypothesis points to another—but rather different from the previous—demand factor. Hypothesis 1 refers to the mix of products and their respective markets, while hypothesis 2 refers to the size of the expected market.

H3: The size and quality of the founding team

New firm lack resources, but they also lack credibility from outside organizations (Stinchcombe, 1965; Baum et al., 2000). The size and quality of the founding team are important factors giving credibility to new firms. It has been demonstrated that performance is linked to the presence of "star scientists" among the founders of the new biotechnology firm (Zucker et al., 1998).

H4: Patenting

Patenting indicates to external organizations that the DBF is conducting innovative R&D. When products are patented, the new biotechnology firm gives the financial and industrial community a signal that she is targeting exclusive new products. When processes are patented, indications are that new, more efficient, more effective or fastest processes, are proprietary to the entrepreneurial firm. Patents thus give credibility to the entrepreneurial biotechnology firm with regard to the financial and industrial community. Venture capitalists see patents as an important landmark, and tend to financially support DBFs that own patents. Alliances are not the only source of credibility to the new biotechnology firm: usually patents come first.

H5: Efficient R&D management

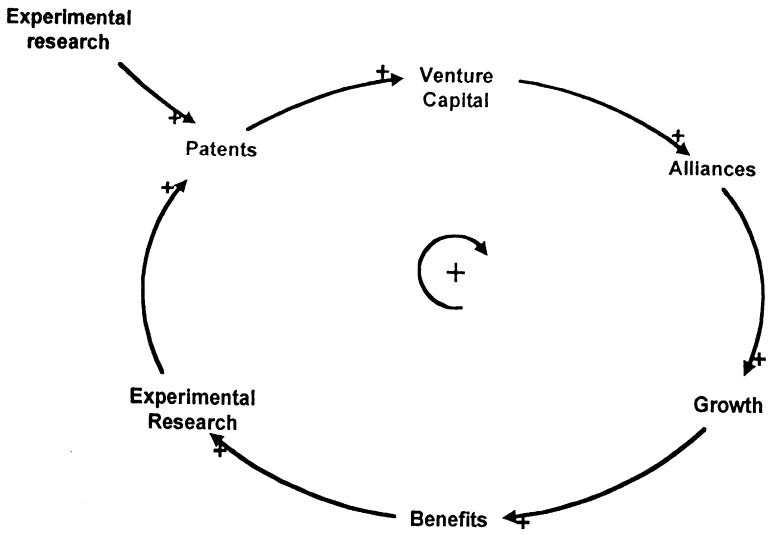
Alliances are not a substitute for efficient and effective internal, in-house R&D (Mowery and Rosenberg, 1989, p. 240). DBFs need some degree of industrial R&D expertise, something different from academic R&D. The goal of industrial R&D is to create new or better products and processes in competition with other business enterprises. Usually, these future products and processes are defended by patents before they arrive into the marketplace (Stephan, 1996). The goal of academic R&D is to produce new general publishable knowledge in competition with other academic research teams. In academic R&D arriving first is a matter of prestige and increased research funds; in business R&D arriving first may be a matter of surviving or disappearing as competition in many of these science-based products are "winner-takes-all" on test. Coming from academia, managers of many DBFs lack the understanding of the difference between two different types of R&D.

H6: Venture capital support

Small new firms lack both capital and credibility. But alliances are not the only source of them. Venture capital usually comes first. Years before DBFs sign multimillion dollars alliances with large pharmaceutical firms, they will need the endorsement of venture capital firms, often for far more reduced amounts. In other words, credibility (and the knowledge base of the DBF) is built through stages. Patents come first, then comes venture capital, then efficient in-house R&D, only then arrive the large corporate allies with their major resources and competencies.

H7: Alliances with sources of fundamental knowledge (universities and government laboratories)

Biotechnology is a science-based activity, where industrial applications are often close to their academic origins. To succeed, firms must keep contact with the sources of constantly evolving basic



Scheme 1. The dynamics of growth in human health biotechnology.

knowledge in an area where the frontier is rapidly moving (Gambardella, 1995).

H8: Alliances with national and international corporations

Finally, designing and launching new biotechnology products is an expensive and complex matter, where the competencies of the DBFs are usually insufficient. Besides financial resources, the competencies of the established corporations in the areas of industrial R&D, governmental approval, manufacturing, and marketing are essential to the success of the small entrepreneurial firm. The previous literature has correctly identified alliances as one key factor of growth in biotechnology. This papers suggests that other milestones come much previously. The whole range of hypothesis is summarized by the Scheme 1.

3. Canadian biotechnology

Canadian biotechnology firms started some years after their American competitors, but taking into account to the size of the country, the share is comparable to its US counterpart. By 1997, according to Statistics Canada, there were some 282 Canadian biotechnology firms. Seventy-one of them were publicly traded. The total market capitalization of these 71 firms was about 12.9 billion Canadian dollars by the end of May 1999. However, the four largest biotechnology firms accounted for two-thirds of that capitalization. Forty-two other firms had a market value of under 50 million Canadian dollars each.

3.1. Dedicated biotechnology firms (DBFs)

Among the 282 DBFs existing in 1997, some 129 were in human health (46%), 62 in agricultural biotechnology, 32 in environment, 20 in food products and 39 in all other areas (Statistics Canada, 1999; BioteCanada, 1999). These 282 firms employed 15,800 people. The human health sector represented over two-thirds of the employees, with an average size of 81 employees, compared to 42 in agricultural biotechnology, 43 in other areas, 22 in environment and 20 in food production. These 282 firms had total revenues of 11.2 billion Canadian dollars including exports for 4.9 billion Canadian dollars.

3.2. Venture capital for biotechnology

The Canadian venture capital market has developed very rapidly in the last 10 years. By the end of 1998, the total venture capital pool was over 8 billion Canadian dollars, and that year more than 1.2 billion Canadian dollars had been invested in some 1200 companies, many of them active in biotechnology.

Seed money was the most frequent type of investment that venture capital firms made in biotechnology companies, the average investment being around 1 million Canadian dollars. With at least 210 firms out of the stock market, it is easy to infer that many demands for venture capital have not been accepted. In other words, even if the Canadian venture capital market is fairly well endowed, it cannot accommodate all the demands from domestic biotechnology firms. A few Canadian companies have obtained foreign funds. In 1999, for instance, two Canadian firms had been financed by US venture capital firms, and another had obtained financing from a British venture capitalist.

3.3. Institutions: NRC and universities

Besides the over 100 venture capital firms operating in Canada, other institutions play a role in the development of Canadian biotechnology. The National Research Council has five laboratories dedicated to biotechnology, the largest of which are the Biotechnology Research Institute of Montreal in human biotechnology, the Plant Biotechnology Institute of Saskatoon (in ag-bio) and Ottawa's Institute for Biological Sciences (in human health). These institutes, created or refurbished in the 1980s and early 1990s, employ several hundred scientists and have modern laboratories where DBFs can conduct or contract out research or obtain licenses. At the same time, some 30 research universities across Canada produce hundreds of doctoral and master's graduates, and thousands of bachelors in biology, biochemistry and related medical and life sciences. It is estimated that one-third of Canadian biotechnology firms are university spin-offs. Also, companies can license technology from university laboratories, and conduct pre-clinical research within them. Finally, several large contract research organizations (CROs) can conduct clinical trials across Canada for a fee.

3.4. The policy environment

In Canada, the legal, regulatory and policy environment is conducive to the development of biotechnology. Companies can obtain refundable tax credits for R&D even if they have no revenues. They can obtain subsidies for research through the Industrial Research Assistance Program (IRAP) managed by the National Research Council since 1962. University researchers can obtain research grants from the Natural Science and Engineering Research Council (NSERC) and the Medical Research Council (MRC), as well as from the federal Centers of Excellence program. These and other direct and indirect government programs can help in the fundamental and applied research phases of the development of a company. The federal government pours not less than 350 million Canadian dollars a year in support of Canadian DBFs.

In Canada as in the United States, new biological entities and drugs need to be approved by governments. Health Canada takes care of drug approval, functional food and neutraceuticals, and genetically-modified organisms (GMOs); Environment Canada supervises and regulates other aspects of new products related to environmental issues.

3.5. Large firms

For historical reasons, there are no Canadian-owned and controlled large pharmaceutical or grain-producing enterprises. All such major corporations operating in the world are American, European or Japanese. If domestic biotechnology firms are to use manufacturing and marketing alliances in order to grow, they must find foreign partners in the United States, western Europe or Japan. Thus, foreign marketing alliances seem mandatory.

4. The study

This study tested some of the above-mentioned hypotheses by building a sample of nearly[1] 30 fast-growing Canadian biotechnology firms, and comparing it with a similar sample of companies experiencing little or no growth. The regional distribution of the companies interviewed appears in Table 1.

The questionnaire used included 25 questions that yielded over 110 variables (see questionnaire attached). The statistical treatment included univariate analysis, correlation and regression, particularly logistic regression, using rapid growth as the main dependent variable. Rapid growth was defined as

[1] Two of the firms that were supposedly growing very fast according to our preliminary database, appeared to be stagnant during the interviews.

Table 1
Regional distribution of companies interviewed

Region	Total sample	Total Canada[a]
Quebec	14 (23%)	86 (30%)
Ontario	12 (20%)	71 (25%)
Prairies	19 (32%)	48 (17%)
BC	9 (15%)	56 (20%)
Maritimes	6 (10%)	20 (7%)
Total	60 (100%)	282 (100%)

[a] Statistics Canada (1999).

Table 2
Product distribution of companies interviewed

Area/product	Total sample	Total Canada[a]
Human health	55%	46%
Ag-bio	28%	22%
Food	7%	11%
Environment	5%	7%
Other	12%	14%
Total	60 (100%)	282 (100%)

[a] Statistics Canada (1999).

growth of 50% and over, either of total employment and/or sales between 1994 and 1998; only firms having crossed the threshold of 25 employees and/or 2 million Canadian dollars in sales qualified as rapid growth enterprises. The main internal capabilities (such as R&D, product targeting and exports) and external capability variables (such as venture capital, alliances and other collaborations) were tested.

4.1. The sample

The sample was composed of firms operating mainly in biotechnology. The median age of the firms in the sample was 10 years old, and only six firms (10% of the sample) were older than 25 years. The median firm had 26 employees and the median sales were 0.6 million Canadian dollars in 1998. Twenty-two companies were public (their shares being listed on the Toronto, Montreal, Alberta, Vancouver and/or NASDAQ stock exchanges). Thirty-eight DBFs were privately owned. Among public companies, the median firm was public since 1994. Also, 90% of the companies interviewed were Canadian-owned and controlled. Out of some 41 rapid growth firms identified through BioteCanada manuals, some 28 were interviewed, 5 refused to collaborate and 8 were out of business by the time we contacted them. Similarly, out of the 40 companies without growth, some 15 refused to collaborate, 8 went bankrupt or merged, and were replaced by other slow- or no-growth firms.

As to the product areas, 55% of the companies (32 firms) were in the area of human health, 28% in ag-bio, 13% in environment, 5% in food and 12% in other sectors. A few companies were active in two areas, which explains that percentages over 100%. This distribution closely matches that of Statistics Canada, where 46% of firms are active mainly in human health, 22% in ag-bio, 11% in environment, 7% in food and 14% in other areas (Statistics Canada, 1999) (see Table 2). No firm, though, had moved from one area to another in the span of its life, but some were working in closely related fields, such as human health and neutraceuticals.

4.2. Descriptive results

All the firms interviewed conducted R&D in Canada with permanent facilities. The hypothesis of R&D and innovation being a key variable in explaining growth was thus rejected, since a constant (R&D activity) cannot explain a variable (growth rates). Also, R&D efforts (measured as a ratio of R&D expenditures to sales) did not correlate with growth. The median R&D personnel in 1998 was 10 employees, and the median R&D expenditure was 1 million Canadian dollars. R&D usually produced patents, but 21 companies had no patents at all, while the median was two patents per firm. Also, 39% of the companies had no products on the market, and the median firm had only one product. Almost two-thirds of the companies exported and for 72% of these firms, the United States was the major market for their exports. western Europe was the first foreign market for 22% of the exporting firms.

Twenty-nine companies (48%) had obtained venture capital, and the median venture capital financing obtained by the firms, usually through more than one round, was 3.5 million Canadian dollars. Two-thirds of the companies in the sample had obtained venture capital in the same province where they had their head office. Among the public companies, the median financing at their initial public offerings (IPOs) was 22 million Canadian dollars and the median market

Table 3
Advantages expected and obtained from alliances

Advantage	Expected	Obtained
Complementary knowledge	39/50 (78%)	36/48 (75%)
Increased speed of innovation	36/49 (74%)	32/48 (67%)
New products	33/50 (66%)	24/44 (55%)
Finance	30/50 (60%)	27/48 (56%)
R&D diversification	28/49 (57%)	26/47 (55%)
Access to larger projects	28/50 (56%)	24/47 (51%)
Marketing	26/50 (52%)	19/45 (42%)
Response to customers	21/49 (43%)	16/46 (35%)
Other advantages	28/49 (57%)	27/48 (56%)

Table 4
Obstacles to growth

Obstacles	All companies	Most important
Access to capital	38/60 (63%)	27/60 (45%)
Access to skilled human resources	33/60 (55%)	11/60 (18%)
Time for regulatory approval	24/60 (40%)	8/60 (13%)
Intellectual property protection	16/60 (27%)	2/60 (3%)
Access to technology	15/60 (25%)	2/60 (3%)
Cost of regulatory approval	14/60 (23%)	4/60 (7%)
Consumer acceptance	14/60 (23%)	3/60 (5%)
Other obstacles	22/60 (37%)	7/60 (12%)

NB: four companies indicated two obstacles as the most important ones.

capitalization by late May 1999 was 43 million Canadian dollars. Most of the companies (16 out of 29 or 57%) that had obtained venture had also received some management services from their venture capital partners. Most of these services consisted of management and financial advice, but one-third of the companies declared having acquired credibility vis-à-vis the biotechnology community—as an intangible externality—from their venture capitalists. In other words, being endorsed by venture capital was a form of recognition in relation to other firms, including future allies.

As found in previous studies, alliances were key for emerging firms that need enormous resources—knowledge, facilities, skilled personnel and capital. It is no surprise then that three quarters of the companies (47/60 or 78%) entered into alliances. By far the most frequent partnerships were aimed at basic research with universities (66% of the firms within alliances had university partners), but 30% of the firms with partnerships had alliances with other companies, aiming at either R&D, manufacturing or marketing. The most common goal of alliances was research, both with university, government laboratories and other firms. A total of 90% of the biotechnology firms with alliances had research alliances, followed by marketing partnerships (33% of the firms with alliances) and manufacturing (31%).[2] A total of 70% of the firms considered alliances and collaborative agreements a major growth factor. Most of them expected and obtained advantages from alliances (see Table 3).

[2] These percentages are all calculated on the firms conducting alliances and the question had non exclusive multiple responses.

The differences between the advantages expected and obtained were usually related to the early stage of the alliance: the expected advantages had not materialized. Not surprisingly, knowledge and increased speed of innovation were the major advantages expected and obtained. After all, most alliances were in the area of R&D. Conversely, as only a few firms had attained the phase of manufacturing and marketing, all advantages related to customers and marketing were lowest on the list. As to “other advantage”, the most frequent consisted in credibility. Partnerships increased the companies’ credibility vis-à-vis the financial and the biotechnology community.

However, one-third (17/48) of the firms involved in partnerships experienced difficulties in alliances. The difficulties included (A) university partners and government organizations had different timeframes and goals: researchers within the alliance wanted to publish, while companies preferred to keep information secret as long as possible. (B) Large industrial partners were usually slow, or had different priorities, or were more bureaucratic and/or did not know the specific technology of the DBF. The latter was by far the most common complaint about alliances.

Obstacles to growth were many. Access to capital and to skilled human resources was by far the most important one (Table 4). High-level managerial and top level scientific talent seems to be in scarce supply in Canada, and these are the skills that companies are looking for. Access to capital was by far the most important obstacle to growth. This is quite understandable, due to the high costs of product development and approvals in biotechnology.

Table 5
Correlation (Pearson)

	Rapid growth	Age	Human health	Patent	Venture capital	Alliance	Foreign alliance	Delay	Public	Consumer acceptance
Rapid growth	1.00									
Age	0.149	1.00								
Human health	0.242	0.252	1.00							
Patent	0.235	0.106	0.337	1.00						
Venture capital	0.052	−0.249	0.223	0.381	1.00					
Alliance	0.330	0.065	0.094	0.136	0.114	1.00				
Foreign alliance	0.185	0.321	0.264	0.218	0.061	0.797	1.00			
Delay	0.139	0.064	0.117	0.043	0.017	−0.068	−0.061	1.00		
Public	0.328	0.006	0.410	0.322	0.100	0.148	0.182	−0.171	1.00	
Consumer acceptance	0.042	0.354	0.055	0.070	−0.072	0.092	0.044	0.072	0.153	1.00
Export	0.237	0.179	0.146	0.088	0.036	0.131	0.233	0.003	0.223	0.122

4.3. Explaining fast growth

A few factors explain rapid growth. I hypothesized that both internal activities and strategies, such as the product area, protection of intellectual property through patents, and exports, as well as external factors, such as venture capital financing and strategic alliances, had an impact on rapid growth. Our data revealed that most companies having experienced rapid growth were older (median of 16 years after foundation), were active in the area of human health biotechnology, had obtained patents and then venture capital, conducted alliances, exported their products and did not experience any obstacle with consumer acceptance. I first correlated some key variables with the dependent one (Table 5). Then I built a logistic regression. (see Table 6).

Age is a main determinant, confirming the fact that in human health biotechnology companies need years of clinical tests to bring discoveries to marketplaces. Ten years seems to be the minimum period required to move ideas from the laboratory to the market. But rapid growth usually requires complex marketing and manufacturing alliances, the negotiation of which usually takes years of mutual accommodation and learning. It is to be underlined that—as almost no firm out of human health was growing—age was not a determinant of growth for these ag-bio or environmental DBFs.

Almost invariably, human health seems to be the sector where rapid growth occurred. It was also the area where firms obtained venture capital more easily. Few firms outside human health experienced fast growth.

Few firms could avoid patenting their inventions. The financial community looks for milestones if it is to invest in new firms without collateral other than ideas. The patent is a sign of the novelty of the firm's idea, thus a condition for future exclusive products. Many firms in our sample omitted to request patents, either because they were afraid of disclosing information and being imitated, or because they considered that requesting and defending patents was too costly, or because they did not considered patents strategic assets. Patents, however, were related to rapid growth.

Exports also affected growth: companies with foreign sales usually experienced rapid growth rates, as they tapped much larger markets, usually the United States or western Europe. No firm targeting only the Canadian market could experience rapid growth. But some firms in ag-bio and environmental biotechnology did in fact target the Canadian market and never tried to export their genetically-modified plants or bacteria. Human health firms were most often targeting the world market. Targeting world markets was, thus, a cause, not simply a consequence of growth, and exports were not always conducted through alliances. The relationship between alliances and exports was weak. Most stagnant companies declared being interested in capturing the Canadian market, that they considered an easier target than international ones. This was particularly true in environmental and agricultural biotechnology. Only one environmental biotechnology firm was in fact growing; it had targeted the US market

Table 6
Explaining rapid growth

Variable	*B*	S.E.	Wald	d.f.	Significance	*R*	Expected *B*
V1	0.0509	0.0371	1.8804	1	0.1703	0.0000	1.052
V5.1	0.9358	0.7331	1.6293	1	0.2018	0.0000	2.5492
V7.1	1.4961	0.9528	2.4657	1	0.1164	0.0817	4.4643
V13.1	0.1088	0.0739	2.1660	1	0.1411	−0.0488	1.115
V14.1	1.4614	0.8197	3.1789	1	0.0746	−0.1300	0.2319
V18	2.108	10.058	3.968	1	0.046	0.0000	8.230
V25.16	−1.5100	1.5371	0.9650	1	0.3259	0.0000	0.2209
Constant	−4.188	1.571	7.105	1	0.008		

Classification table for V3.6 (the cut value is 0.50)

Observed growth	Predicted		
	Yes	No	
Rapid	16	6	72.73%
Not rapid	4	25	86.21%
Overall			80.39%
	χ^2	d.f.	Significance
Model	18.719	7	0.0091
Block	18.719	7	0.0091
Step	18.719	7	0.0091

−2 Log likelihood: 51.018; Goodness-of-fit: 84.783; Cox and Snell: 0.307; Nagelkerke: 0.412. V1: AGE (number of years after foundation); V5.1: HHEALTH (products targeted for human health); V7.1: EXPORT (company exports products, Yes/No); V13.1: PATENT (company has patents, Yes/No); V14.1: VENCAP (company obtained venture capital, Yes/No); V18: ALLIANCE (company conducts alliances, Yes/No); V25.16: CONSAC1 (consumer acceptance is major problem for those not growing); V3.6: RAGRO (rapid growth, our dependent dichotomic variable).

in its strategic plan, through the acquisition of a US subsidiary possessing US patents. Most ag-bio firms targeted the Canadian market.

It is clear, though, that for growth to be maintained, feedback effects need to take place between growth and exports, a well-known phenomenon in business dynamics. The labeling of the responses showed that targeting export markets was necessary to obtain (and preceded) venture capital and international business alliances.

Alliances appeared as the major determinant of growth. The Expected *B* figures of Table 6 show that they explain almost 50% of the probability of rapid growth. However, Expected B figures show that the other variables taken together are more important than alliances in explaining growth. In other words, alliances are not enough: exports, specialization in human health products, age and venture capital, are as important as alliances in explaining rapid growth.

The timing of alliances was also important. Some alliances arrived too early, and the biotechnology firm could not profit from its innovation, because it negotiated a partnership before the full value of its novelty could be properly evaluated. Cash-strapped firms usually signed early alliances only to discover later that the larger partner appropriated most of the benefits. The best sequence of events occurred when the biotechnology firms had enough capital to complete their Phase III trials, or their field trials, and then organized alliances with foreign partners. Thus, alliances were a necessary condition of growth only if properly managed.

Finally, consumer acceptance was not a problem for most human health firms. often in the fast growth track. Problems with GMOs affected a large proportion of the environmental and agricultural biotechnology firms. Most of the human health enterprises, and a few niches in ag-bio and food (especially

Table 7
Rapid growth and major product areas

	Rapid growth		
	Yes	No	Total
Human health[a]			
Yes count	19	9	28
Percentage with rapid growth	68%	32%	100%
Percentage in human health	58%	33%	47%
Percentage of total	32%	15%	47%
No count	14	18	32
Percentage with rapid growth	44%	56%	100%
Percentage in human health	42	67%	53%
Percentage of total	23%	30%	53%
Total count	33	27	60
Percentage of total	55%	45%	100%
Ag-bio[b]			
Yes count	7	21	28
Percentage with rapid growth	25%	75%	100%
Percentage in ag-bio	41%	49%	47%
Percentage of total	12%	35%	47%
No count	10	22	32
Percentage with rapid growth	32%	69%	100%
Percentage in ag-bio	59%	51%	53%
Percentage of total	17%	37%	53%
Total count	17	43	60
Percentage of total	28%	72%	100%

NB: two of the firms that the preliminary database had identified as experiencing rapid growth, were in fact, stagnant according to the interviews.

[a] Fisher's exact test (two sided) significance = 0.074; one sided = 0.053.

[b] Fisher's exact test (two sided) significance = 0.775; one sided = 0.403.

Table 8
Venture capital by major product area

	Venture capital obtained		
	Yes	No	Total
Human health[a]			
Yes count	19	13	32
Percentage within human health	59%	41%	100%
Percentage with venture capital	66%	43%	54%
Percentage of total	32%	22%	54%
No count	10	22	32
Percentage within human health	37%	63%	100%
Percentage with venture capital	35%	57%	46%
Percentage of total	17%	29%	46%
Total count	29	30	59
Percentage of total	49%	51%	100%
Ag-bio[b]			
Yes count	6	11	17
Percentage within ag-bio	35%	65%	100%
Percentage with venture capital	21%	37%	29%
Percentage of total	10%	19%	29%
No count	23	19	42
Percentage within ag-bio	55%	45%	100%
Percentage with venture capital	79%	63%	71%
Percentage of total	39%	32%	71%
Total count	29	30	59
Percentage of total	49%	51%	100%

[a] Fisher's exact test (two sided) significance = 0.119; one sided = 0.073.

[b] Fisher's exact test (two sided) significance = 0.252; one sided = 0.143.

neutraceuticals) were unaffected by negative consumer reception of their products.

Out of 32 firms operating in human health, 19 attracted venture capital (59%) and also 19 experienced rapid growth. Most of them had alliances, including with the goal of manufacturing and marketing. Conversely, out of seven companies in environment, only three firms obtained venture capital and only one of these experienced rapid growth. None of them became public or conducted major alliances. Table 7 shows how differently the major product areas behaved in terms of rapid growth.

In agricultural biotechnology, out of 17 companies interviewed, 7 experienced rapid growth (41%) and 10 did not (59%). While human health companies represented 68% of firms with rapid growth, agricultural biotechnology represented another 25%, environmental biotechnology 3% (only one firm) and food products, basically neutraceuticals, 6% (two firms). None of the companies operating in other product areas experienced rapid growth.

The difficulties experienced by the environmental firms were clearly expressed by at least one interviewee when he stated that venture capital was virtually non existent in this area. Conversely, human health companies had more ample access to venture capital. Tables 8 and 9 summarizes some relevant data about venture capital by major product areas.

Table 7 shows that 59% of the human health firms had obtained venture capital, and that they represented

Table 9
Obstacles to growth in firms with slow or no growth

Obstacles	Is an obstacle	The most important obstacle
Access to capital	21/32 (66%)	19/32 (59%)
Access to skilled human resources	16/32 (50%)	4/32 (13%)
Time for regulatory approval	12/32 (38%)	3/32 (9%)
Intellectual property protection	9/32 (28%)	0/32 (0%)
Consumer acceptance	8/32 (25%)	2/32 (6%)
Cost of regulatory approval	6/32 (19%)	1/32 (3%)
Access to technology	5/32 (16%)	1/32 (3%)
Other obstacles	12/32 (38%)	3/32 (9%)

two-thirds of the firms with venture capital within the total sample. Conversely, only 35% of the agricultural biotechnology firms in the sample obtained venture capital, and that they counted for only 21% of the firms with venture capital in the sample (but ag-bio represented 28% of the sample's firms). In other words, human health firms obtain venture capital more easily than any other category.

Against all expectations, some variables were not significant. Public companies did not fare much better than private ones. Several factors explain this surprising result. First, some large public companies knew major delays in product development due to wrong product targeting, unexpected difficulties linked to the complexity of the organisms they were working on, or more simply, inefficient research and development organizations. Second, some companies went public, but collected only a few million dollars through their IPOs. In several cases, the results of the IPO were not larger than the sums they would have obtained through venture capital or private placements. Also, being public imposes costs, particularly disclosure, public relations, communication and legal costs. Some companies thus had all the disadvantages of being public without the advantages of having access to a large capitalization.

Other logistic regressions (not presented in this paper for reasons of space) showed similar results, but added new dimensions. Foreign alliances had a better chance than any other type of alliances of predicting rapid growth. Foreign alliances were almost invariably conducted with large international corporations for manufacturing and marketing products, as opposed to domestic ones, which were essentially conducted with university and government laboratories. Also, avoiding R&D delays improved the regression results: the quality of R&D management counted in the efficient use of scarce financial resources.

It is clear that rapidly growing firms may attract large international allies. However, the "virtuous" sequence showed that small companies in human health owning patents and having obtained venture capital were more prone to sign alliances and then start their rapid growth processes. Alliances brought usually much more funds (in the dozens or hundreds of millions of dollars) to the DBFs than most IPOs (on average around 15 million Canadian dollars) and most venture capital financing (usually in the average of 1.5 million Canadian dollars); this is why alliances preceded rapid growth. They brought to the DBFs the resources needed for growth.

5. Conclusion

In the last 25 years, biotechnology has emerged to capitalize on the extraordinary development of molecular biology, genetics and biochemistry, which took place in the postwar period. Several thousand companies across the world, including over 300 in Canada, have created or are developing hundreds of new therapeutic compounds, diagnostic kits as well as genetically-modified plants, bacteria and animals. However, the cost of such new products and GMOs is staggeringly high, and most DBFs are financially strained. Only a few of these new firms will grow, provided they adopt the right strategies and mix of products.

In Canada, rapid growth is associated with a certain age of the biotechnology firm, usually over 10 years. Also, the growing firms usually operated in the area of human health products, an area without the problems of consumer acceptance that plague environment, food and agricultural biotechnology. Fast-growing enterprises adopted a strategy of patenting major novelties, searched and obtained venture capital financing, and targeted large markets by exporting their products, usually through alliances with foreign pharmaceutical corporations. Internal R&D capabilities

avoided delays in delivering their products, or in moving results from one phase to the next.

The following empirical conclusions can also be drawn from this study.

1. *Markets and increasing returns*: These are knowledge-intensive products subject to economies of scale (it pays to produce the knowledge once and to sell it embodied as many times as possible). Going for export markets seems unavoidable. Appiah-Adu and Ranchhod (1998) have found that market orientation was a key factor of growth. We found that only international market orientation was positively related to rapid growth.
2. *The many roles of venture capital*: It has been underlined several times that venture capital firms provide funds to DBFs as well as management and financial competencies. Venture capital firms force the DBFs to adopt advanced management routines in critical areas such as R&D, marketing and manufacturing. Also, venture capital will search the best conditions to launch the firm in the stock market in order to insure a profitable exit for itself and at the same time a more solid financial position for the DBF. This study found that venture capital also brings credibility to the DBF, particularly with regard to potential allies, as well as other venture capital firms that may contribute in future, and more expensive financial rounds. Venture capital firms have avoided all areas of biotechnology except human health. Thus the strong relationship between the human health niche, patents, venture capital and public offerings.
3. *Timing alliances*: Alliances may provide substantial resources to emergent biotechnology companies. However, alliances are not always successful. Too early an alliance can lead to contracts where the biotechnology firm loses most of the benefits of its innovation because of the low valuation of underdeveloped intellectual property assets, but conversely it can help a cash-strapped firm to survive. On the other hand, if the alliance comes too late, the biotechnology firm may already find itself in a weak position due to cash flow problems. We found that rapid-growing biotechnology firm usually start obtaining venture capital and access to the capital market to finance their R&D projects, and postpone large commercial partnerships to the end of Phase III clinical trials or field tests, when their products are already tested and approved. This finding elucidates the empirical literature showing that the benefits of alliances may be unevenly distributed among partners according to a variety of conditions (Lerner and Merges, 1997).

Some issues were suggested by the interviews. At least two of them are important to mention. First, patents are a way through which DBFs send signals to the financial community about the novelty of their future products, thus about their exclusive rights to some useful new technology, and the related high profits that are often associated with a unique technology. Venture capital uses this signal to allocate funds to DBFs, and venture capital is a major growth factor in biotechnology, as it gives these firms financial resources and credibility.

The general empirical finding that emerging from this study is that, in a very competitive market, where hundreds of biotechnology enterprises struggle for capital with other high-technology enterprises, the emerging biotech companies should proceed through a sequence of almost unavoidable milestones. The sequence starts with obtaining patents. These will signal to the financial community the value of the new firm. Patenting is followed by venture capital, efficient R&D, entry into the stock market under the guidance of the venture capital firm, and the organization of a major alliance followed by the launching of the firm's products in the overseas market, usually with the help of large international corporate partners. Nine out of 28 DBFs with rapid growth had followed that pattern. Only four firms with rapid growth had signed alliances with other firms, and had obtained neither patents nor venture capital: two of them were subsidiaries of foreign pharmaceutical corporations, and two others were producers of bio-fertilizers. Twenty-three firms with rapid growth needed both alliances and something more in order to grow, usually patents or venture capital, but not always in the order that the sequence postulated here suggests.

Scheme 1, thus, suggests the most complete sequence of milestones. However, some of the milestone of this sequence could eventually be skipped. A few of the rapid-growing firms did not actually own patents, but were instead the beneficiaries of exclusive licenses from research universities. A few of the fast

growing DBFs had not received venture capital but moved, due to the high-quality of their patents and scientists, moved directly from patents to alliances. However, most frequently these rapidly-growing firms had moved from one to the other of all these milestones before they had achieved rapid growth (see Scheme 1).

Our results confirm most of our hypotheses. These findings bring some confirmation to both internal growth and competence theories of the firm, as well as to external growth and evolutionary perspectives. Targeting the right niche from the start, patenting, conducting efficient R&D and exporting are all in the area of firm strategy and are related to managerial competencies. R&D and innovation as such, because they are pervasive, are not exclusive to rapid growth companies. Product development efficiency, though, is related to fast growth. The importance given to skills as a major obstacle to growth also brings some support to internal growth theories, even in the original formulation by Edith Penrose: top managers are in short supply, and limit the growth of the firm. But, as evolutionary theories suggest, firms that have built capabilities in one area (such as genetically-modified bacteria for environmental purposes) will not easily move into another area (such as human health products) even if they are aware of the reluctance of venture capital to fund them. DBFs often live and stagnate (or grow) with their "genes", as suggested by the ecological perspective.

External growth theories also receive strong confirmation: access to capital, usually obtained either through venture capital and/or strategic alliances, is a major growth factor. The vast majority of the firms considered that both alliances and venture capital were major growth factors. The statistical analysis brings additional evidence in favor of this perspective: both variables contribute to explain rapid growth. Marketing alliances with overseas partners in the United States and/or western Europe seemed mandatory for companies having completed the development of their products. However, all alliances did not necessarily succeed, and the declining support and/or interest of their partners sometimes disappointed DBFs. Also, all alliances are not equally strategic for long-term growth. This finding brings a subtle nuance to the many studies (Pisano, 1991; Barley et al., 1992; Powell et al., 1996) that have shown the pervasiveness of alliances and networks in biotechnology. In their beginnings, DBFs organize partnerships with universities and government laboratories, but these early alliances only help them to bring new knowledge to the research project. In other words, all alliances and networks are not equally valuable for the DBFs: long-term rapid growth is mostly related to manufacturing and marketing alliances, where large partners bring more diverse and costly resources and competencies to the DBF, in the areas of clinical testing, regulatory approvals, production and international marketing.

In summary, all networks and alliances are not conducive to growth. This result qualifies the abundant network explanations of the dynamics of biotechnology. Interaction with research universities and government laboratories is almost always present in biotechnology start-ups. But success (as measured by growth) is linked to the financial support of venture capital and large corporate partners.

One major theoretical conclusion is that resource-based, competence and evolutionary approaches can be used simultaneously in the study of a high-technology activity such as biotechnology. While idiosyncratic competencies and resources help to explain the specific endowments of firms and their divergent growth rates, evolutionary approaches help through their accent on successful internal (R&D) and external (alliance) routines and environmental forces shaping the performance of organizations.

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References

Appiah-Adu, K., Ranchhod, A., 1998. Market orientation and performance in the biotechnology industry: an exploratory empirical analysis. Technology Analysis and Strategic Management 10 (2), 197–210.

Arthur, W.B., 1994. Increasing Returns and Path Dependence in the Economy. University of Michigan Press, Ann Arbor.

Barley, S.R., Freeman, J.H., Hybels, R.C., 1992. Strategic alliances in commercial biotechnology. In: Nohria, N., Eccles, R.G. (Eds.), Networks and Organizations. Harvard Business School Press, Boston, pp. 311–347.

Bartholomew, S., 1997. National systems of biotechnology innovation: complex interdependence in the global system. Journal of International Business Studies 28 (2), 241–266.

Baum, J.A.C., Calabrese, T., Silverman, B.R., 2000. Don't go it alone: alliance network composition and start up performance in Canadian biotechnology. Strategic Management Journal 21, 267–294.

BioteCanada, 1993, 1995, 1998, 1999. Canadian Biotechnology Directory, Ottawa.

Cooper, R.G., 1998. Product Leadership. Perseus, Reading.

Das, T.K., Teng, B.S., 2000. A resource-based theory of strategic alliances. Journal of Management 26 (1), 31–61.

Eisenhardt, K., Schoonhoven, C., 1990. Organizational growth: linking founding team, strategy, environment, and growth among US semiconductor ventures, 1978–1988. Administrative Science Quarterly 35, 504–529.

Enright, M., 1998. Regional clusters and firm strategy. In: Chandler, A.D., Hagstrom, P., Solvell, O. (Eds.), The Dynamic Firm. Oxford University Press, New York, pp. 315–342.

Foss, N. (Ed.), 1997. Resources, Firms and Strategies. Oxford University Press, New York.

Foss, N., Knudsen, C. (Eds.), 1996. Towards a Competence Theory of the Firm. Routledge, London.

Gambardella, A., 1995. Science and Innovation. Cambridge University Press, Cambridge.

Gulati, R., 1998. Alliances and networks. Strategic Management Journal 19, 293–317.

Hamel, G., Heene, A., 1994. Competence-Based Competition. Wiley, Chichester.

Hamel, G., Prahalad, C.K., 1994. Competing for the Future. Harvard Business School Press, Boston.

Kenney, M., 1986. Biotechnology: The University-Industrial Complex. Yale University Press, New Haven.

Lerner, J., Merges, R., 1997. The Control of Strategic Alliances: An Empirical Analysis of Biotechnology Collaborations. NBER Working Paper # 6014, Cambridge, MA.

McKelvey, M., 1996. Evolutionary Innovation: Early Industrial Uses of Genetic Engineering. Oxford University Press, Oxford.

Mowery, D.C., Rosenberg, N., 1989. Technology and the Pursuit of Economic Growth. Cambridge University Press, Cambridge.

Mytelka, L., 1999. New trends in biotechnology networking. International Journal of Biotechnology 1 (1), 30–41.

Nelson, R.R., 1995. Why do firms differ and why does it matter? In: Rumelt, R.P., Schendel, D.E., Teece, D.J. (Eds.), Fundamental Issues in Strategy. Harvard Business School Press, Boston, pp. 247–270.

Niosi, J., 1995. Flexible Innovation. McGill-Queen's University Press, Montreal.

Niosi, J., 2000. Science-based industries: a new Schumpeterian taxonomy. Technology in Society 22, 429–444.

Penrose, E., 1959. The Theory of the Growth of the Firm. Basil Blackwell, Oxford.

Pisano, G., 1991. The governance of innovation: vertical integration and collaborative agreements in the biotechnology industry. Research Policy 20, 237–249.

Powell, W.W., Brantley, P., 1992. Competitive cooperation in biotechnology: learning through networks? In: Nohria, N., Eccles, R.G. (Eds.), Networks and Organizations. Harvard Business School Press, Boston, pp. 366–393.

Powell, W., Koput, K.W., Smith-Doer, L., 1996. Inter-organizational networks and the locus of innovation: networks of learning in biotechnology. Administrative Science Quarterly 41, 116–145.

Powell, W., 1999. The social construction of an organizational field: the case of biotechnology. International Journal of Biotechnology 1 (1), 42–66.

Prevezer, M., 1998. Clustering in biotechnology in the USA. In: Swan, G.M.P., Prevezer, M., Stout, D. (Eds.), The Dynamics of Industrial Clustering. Oxford University Press, New York, pp. 124–193.

Rumelt, R.P., 1991. How much does industry matter? Strategic Management Journal 12, 167–185.

Ryan, A., Freeman, J., Hybels, R., 1995. Biotechnology firms. In: Carroll, G.R., Hannan, M.T. (Eds.), Organizations in Industry. Oxford University Press, New York, pp. 332–358.

Senker, J., 1996. National systems of innovation, organizational learning and industrial biotechnology. Technovation 16 (5), 219–230.

Statistics Canada, 1999. Canadian Biotechnology Statistics, Ottawa.

Stephan, P., 1996. The economics of science. Journal of Economic Literature XXXIV, 1199–1235.

Stinchcombe, A.L., 1965. Social structure and organizations. In: March, J.G. (Ed.), Handbook of Organizations. Rand McNally, Chicago, pp. 142–193.

Wald, S., 1996. Introduction. STI Review, OECD, Special issue on biotechnology, Paris, pp. 7–19.

Zucker, L., Darby, M., Brewer, M.B., 1998. Intellectual human capital and the birth of US biotechnology enterprise. American Economic Review 88 (1), 290–306.