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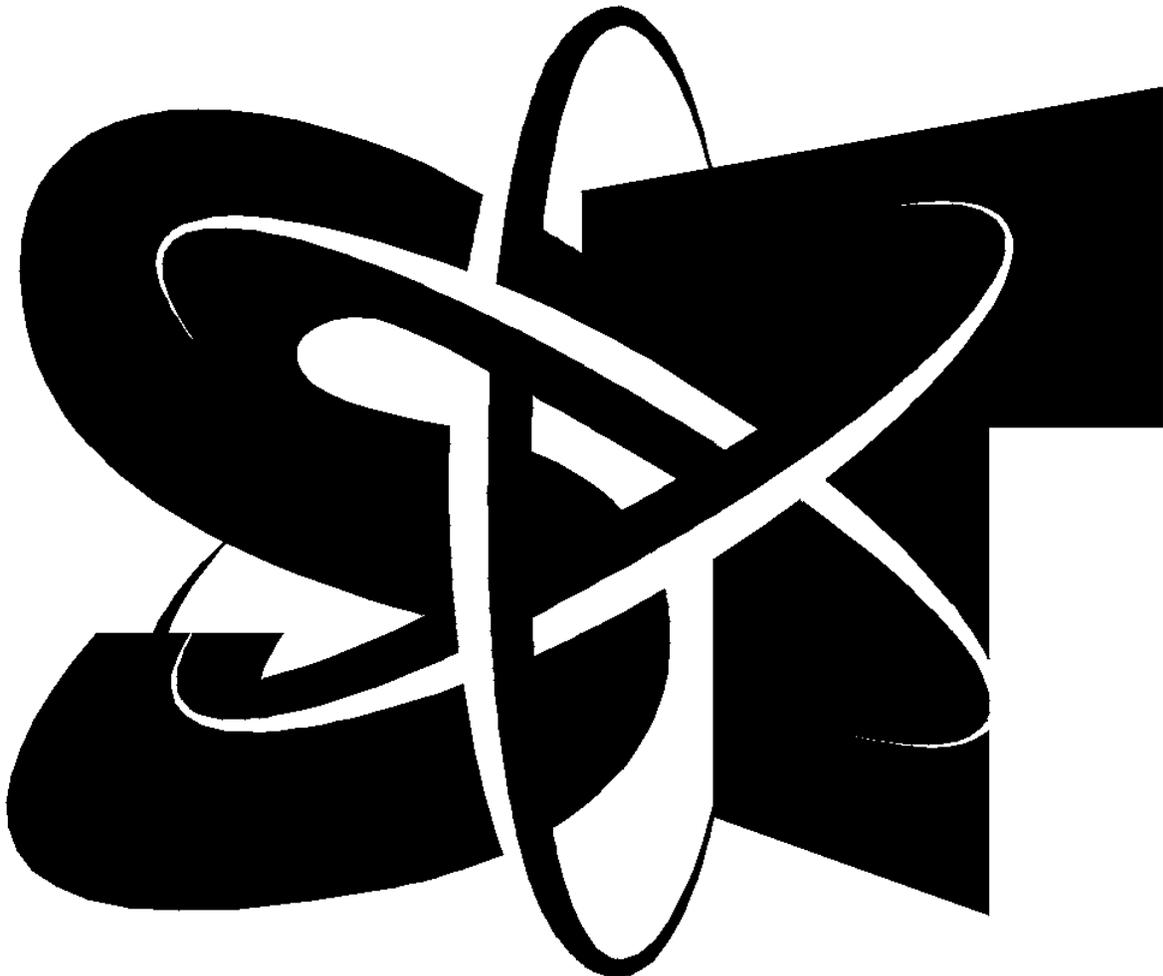
Projet de remaniement  
des sciences et de la technologie

**Document  
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**EXPLAINING RAPID GROWTH IN  
CANADIAN BIOTECHNOLOGY FIRMS**

Jorge Niosi

No. 8



*Sciences & Technologies*



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# **Explaining Rapid Growth in Canadian Biotechnology Firms**

**Jorge Niosi**

Professor  
Département Management et technologie  
Université du Québec à Montréal  
(UQAM)

and  
Researcher  
CIRANO

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## The Science and Innovation Information Program

The purpose of this program is to develop **useful indicators of science and technology activity** in Canada based on a framework that ties them together into a coherent picture. To achieve the purpose, statistical indicators are being developed in five key entities:

- **Actors:** are persons and institutions engaged in S&T activities. Measures include distinguishing R&D performers, identifying universities that license their technologies, and determining the field of study of graduates.
- **Activities:** include the creation, transmission or use of S&T knowledge including research and development, innovation, and use of technologies.
- **Linkages:** are the means by which S&T knowledge is transferred among actors. Measures include the flow of graduates to industries, the licensing of a university's technology to a company, co-authorship of scientific papers, the source of ideas for innovation in industry.
- **Outcomes:** are the medium-term consequences of activities. An outcome of an innovation in a firm may be more highly skilled jobs. An outcome of a firm adopting a new technology may be a greater market share for that firm.
- **Impacts:** are the longer-term consequences of activities, linkages and outcomes. Wireless telephony is the result of many activities, linkages and outcomes. It has wide-ranging economic and social impacts such as increased connectedness.

The development of these indicators and their further elaboration is being done at Statistics Canada, in collaboration with other government departments and agencies, and a network of contractors.

Prior to the start of this work, the ongoing measurements of S&T activities were limited to the investment of money and human resources in research and development (R&D). For governments, there were also measures of related scientific activity (RSA) such as surveys and routine testing. These measures presented a limited picture of science and technology in Canada. More measures were needed to improve the picture.

Innovation makes firms competitive and we are continuing with our efforts to understand the characteristics of innovative and non-innovative firms, especially in the service sector that dominates the Canadian Economy. The capacity to innovate resides in people and measures are being developed of the characteristics of people in those industries that lead science and technology activity. In these same industries, measures are being made of the creation and the loss of jobs as part of understanding the impact of technological change.

The federal government is a principal player in science and technology in which it invests over five billion dollars each year. In the past, it has been possible to say only *how much* the federal government spends and *where* it spends it. Our report **Federal Scientific Activities, 1998 (Cat. No. 88-204)** first published socio-economic objectives indicators to show *what* the S&T money is spent on. As well as offering a basis for a public debate on the priorities of government spending, all of this information has been used to provide a context for performance reports of individual departments and agencies.

As of April 1999, the Program has been established as a part of Statistics Canada's Science, Innovation and Electronic Information Division.

The final version of the framework that guides the future elaboration of indicators was published in December, 1998 (**Science and Technology Activities and Impacts: A Framework for a Statistical Information System**, Cat. No. 88-522). The framework has given rise to **A Five-Year Strategic Plan for the Development of an Information System for Science and Technology** (Cat. No. 88-523).

It is now possible to report on the Canadian system on science and technology and show the role of the federal government in that system.

Our working papers and research papers are available at no cost on the Statistics Canada Internet site at <http://www.statcan.ca/english/research/scilist.htm>.

## **CONTACTS FOR MORE INFORMATION**

### **Science, Innovation and Electronic Information Division**

Director                      Dr. F.D. Gault    (613-951-2198)

Assistant Director        Brian Nemes    (613-951-2530)

Assistant Director        Paul McPhie    (613-951-9038)

### **The Science and Innovation Information Program**

Chief, Indicators Development

Dr. Frances Anderson (613-951-6307)

Chief, Knowledge Indicators

Michael Bordt            (613-951-8585)

Chief, Innovation

Daood Hamdani        (613-951-3490)

Chief, Life Science Unit

Antoine Rose            (613-951-9919)

### **Science and Innovation Surveys Section**

Chief

Bert Plaus                (613-951-6347)

Senior Project Officer

Don O'Grady            (613-951-9923)

Senior Project Officer

Janet Thompson        (613-951-2580)

**FAX: (613-951-9920)**

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## **EXECUTIVE SUMMARY**

This report is the result of an empirical exploratory study, conducted with the support of Statistics Canada in the summer 1999. The goal of the research was to understand the factors explaining the rapid growth of a small number of biotechnology firms in Canada. For that purpose, some sixty firms were interviewed across the country. We tried to find and join some thirty companies experiencing rapid growth (growth of 50% and over, of total employment and/or sales, between 1994 and 1998, and having crossed the threshold of twenty-five employees and/or \$2 million in sales). I interviewed twenty-eight of those firms and a control group of thirty-two firms with slow growth or no growth at all.

A few variables explained much of the fast growth. These were the age of the firm (growing firms were typically over ten years old), the strategy of targeting human health products, patenting their novelties, obtaining venture capital, organizing alliances and particularly with overseas private firms, exporting, and not being confronted with consumers acceptance problems.

## 1. Introduction

Biotechnology is one of the three generic technologies that surged in the Post war period, together with information technologies and advanced materials. Biotechnology has several distinctive traits that differentiate it from the two other ones.

In the first place, from a chronological point of view, it is the latest to be developed, the first company, Genentech, having started only in 1976. Today there are some 3500 dedicated biotechnology companies in the world, including 1350 in the United States, 750 in Continental Europe, 450 in the United Kingdom and some 300 in Canada. At least fifty per cent of those companies are in the area of human health. The second most important application is agricultural biotechnology, followed by food, environment and other areas, such as aquaculture, bio-informatics and specialized chemicals.

Second, research and development in biotechnology, particularly in the area of human health, is a very costly activity. Some authors calculate that the total cost of pre-clinical research, compound characterization and the three phases of clinical essays, and governmental approvals necessary to launch a new medical compound in the market is US\$500 million today, including the costs of failures and marketing (Drew, 1999). Other estimates put pre-clinical research at 0,2 to 0,8 US\$ million, phase I clinical essays at 5 to 10 US\$ million, Phase II trials at 10 to 50 US\$ million, and Phase III essays at 50 to 200 US\$ million. The cost varies according mainly to the type of human health product (diagnostic kits, vaccines, chemical compounds or gene therapy). Diagnostic kits are less costly to develop than new vaccines or drugs, but they address themselves to smaller markets. Also, the three phases of clinical trials are lengthy: they take between five and ten years. When it comes to approvals, they require several thousands of pages and up to 250 000 pages in the United States describing the clinical tests (Drew, 1999). The preparation of the request to the Federal Drug Administration or to Health Canada takes at least one year. No company thus can launch a new health product without having spent from US\$ 50 million to 500 million and worked for five to twelve years. As nearly 2000 human health companies across the world are operating in this area, and they have from four to seven products each in the R&D pipeline, this sector of biotechnology alone requires hundreds of billions of dollars to develop their products. In other words, due to the rapid development of the science base in molecular biology, genetics and biochemistry, thousands of new drugs, vaccines, and diagnostic kits are now waiting to be financed. Most of them will not. Thus there is an enormous demand for venture capital and financial resources from the human biotechnology community towards the financial sector and large pharmaceutical corporations. As the president of Biogen put it bluntly, in 1997, the entire capitalization of human health biotechnology firms was US\$ 100 billion. These firms spend \$US 10-11 billion a year in R&D, while a large pharmaceutical company like Merck has a market capitalization of \$US 150 billion and spends US\$2 billion annually (Tobin, 1998). Finally the costs of producing and marketing the new compounds is also very substantial, particularly considering the fact that after ten years of clinical development, half of the period of patent protection has already passed. Firms have only ten years to recuperate their investment in R&D. Manufacturing and marketing have to proceed swiftly if the new compound is to bring some return to the investors. Only large pharmaceutical firms have the resources and capability to manufacture and sell in large scale a new drug. Strategic alliances with large pharmaceutical corporations are thus mandatory for the small biotechnology company. And accessing the capital market with an initial public offering (IPO) will not be enough if this does not bring to the emerging company a minimum of 50 US\$ million to cover at least Phase II trials.

Fourth, spin-off firms from academia and research institutes immediately invested the new technology, as scientists were the first to recognize the industrial potential of the new discoveries. This is why most of the new technology was controlled at the start by thousands of new firms. However, big pharmaceutical, chemical and other large corporations adopted the new technology later, but with much greater resources. Thus large and small corporations compete today to capitalize on the new scientific discoveries.

Fifth, this technology is mostly diffused in knowledge-intensive industries. In these industries, the optimal exploitation of an expensive invention is through the larger production volumes, as the R&D and marketing expenditures represent most of the total production cost. In other words these are increasing returns industries (Arthur, 1994). Also, even if protected by patents, these products are more easily imitated than those whose production is sheltered by huge capital investments in manufacturing facilities, such as bulk chemicals or primary metals. Thus investments on pharmaceutical products, transgenic plants and animals (like those on software programs or semi-conductors) are better recuperated through rapid innovation and marketing.

When it comes to agricultural biotechnology, again, barriers to growth of start-ups are formidable. Many small and medium-sized enterprises (SMEs) have been able to develop transgenic plants, such as new varieties of canola, maize or tomatoes, but the large agro-business corporations have also managed to develop new plant varieties incorporating desirable characteristics such as resistance to pests. These corporations are able to sell their new

varieties to the farmers across the world, something the biotechnology SMEs can not do. Again, alliances with large agro-business corporations to commercialize the new plants are mandatory for the biotechnology start-up. Even if the costs of developing a new transgenic plant are not so high as in human health, field tests have to be conducted in different environments in order to guarantee the viability of the new organism. The costs of such field trials may also be in the millions of dollars depending on the plant (Bunders et al., 1996; Mann, 1999).

But another hurdle appears in front of the ag-bio firms, namely increasing consumers' resistance, particularly in Western Europe, against genetically modified organisms (GMOs), be they plants or animals. Increasingly, consumers are requiring to be informed about the precise content of the food products they acquire. Also, farmers are afraid of "contamination" of existing plants and weeds by genes added to transgenic plants, making them resistant to pesticides or insects, but having unwanted effects on other insects than the pests they were meant to combat. The rise of agricultural biotechnology has been meteoric: in 1996 the first transgenic seed was widely distributed; in 1999 over 50 million hectares worldwide are planted with genetically modified crops (Mann, 1999). The United States, Canada, China and Argentina are the most enthusiastic adopters of the new technology. Opposition to GMOs is greater in Western Europe.

Consumers' resistance is at its maximum level when it comes to modified bacteria used for environmental purposes, such as cleaning up mining or oil sites, or composting household waste. As no researcher or biotechnology firm can guarantee how the new bacteria will mutate, or interact with other microorganisms, consumers are wary about the introduction of genetically modified bacteria in their environment.

## 2. Canadian biotechnology

Canadian biotechnology started some years after their American competitors, but due account to the size of the country, it is comparable to the US movement. By 1997, there were some 282 Canadian biotechnology firms, and seventy-one of them were public. The total market capitalization of these seventy-one firms was about 12,9 C\$ billion 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 under 50 C\$ million each. Ten of them had a market value of less than 10 C\$ million. Also, the window of opportunity seemed to be closing for biotechnology IPOs: in the first six months of 1999 only one new Canadian biotechnology firm reached the market with an offer that collected 22 C\$ million.

### 2.1 The dedicated biotechnology firms (DBFs)

Among the 282 DBFs existing in 1997, some 129 were in human health (46%), 62 in agricultural biotechnology, thirty-two in environment, twenty in food products and thirty-nine in all other areas. These 282 firms employed 15800 people. The human health sector represented over two-thirds of the employees, with an average size of eighty-one employees, against forty-two in agricultural biotechnology, forty-three in other areas, twenty-two in environment and twenty in food production. These firms had total revenues of 11,2 C\$ billion including exports for 4,9 C\$ billion.

### 2.2 Venture capital for biotechnology

The Canadian venture capital market has developed very rapidly in the last ten years. By the end of 1998 the total venture capital pool was over 8 C\$ billion, and that year more than 1,2 C\$ billion had been invested in some 1200 companies, sixty of them been 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 C\$ million. With some 210 firms out of the capital market, it is easy to calculate that many demands for venture capital have not been accepted. In other words, even if the Canadian venture capital market is fairly well provided, it can not accommodate all the demands from the domestic biotechnology firms.

### 2.3 Institutions: NRC and universities

Besides the over one hundred 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 being 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, employ several hundreds of scientists and possess modern laboratories where DBFs can conduct research or obtain licenses. At the same time, some thirty 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.

## 2.4 The policy environment

In Canada the legal, regulatory and policy environment is much 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.

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 nutraceuticals and GMOs, and Environment Canada of other aspects and new entities related to environmental issues.

## 2.5 The large firms

For historical reasons, there are no Canadian owned-and -controlled large pharmaceutical or grain producing enterprises. All these large corporations are either American, European or Japanese. If Canadian biotechnology firms are to use manufacturing and marketing alliances in order to grow, they will necessarily find foreign partners in the United States, Western Europe or Japan.

# 3. Theory: the growth of the small firm

## 3.1 The preceding literature

The differential growth of enterprises was the central concern of Edith Penrose (1959) in her seminal work on the theory of the growth of the firm. She postulated that differential growth was the result of internal resources and activities, particularly management capabilities and behaviour. Her work has founded one of the most influential currents of management thought in the last twenty years: the resource-based and competencies theories of the firm (Hamel and Prahalad, 1994; Hamel and Heene, 1994; Foss and Knudsen, 1996; Foss, 1997). In these theories, growth is seen as dependent on internal capabilities of the firm, including R&D, managerial and marketing capabilities. In a major study on Canadian small and medium-sized enterprises and factors behind their growth, Baldwin (1996) has emphasized R&D and innovation activities, managerial capabilities and marketing strategies, including exports.

Another strand of theories has put the accent on external factors of growth. In the area of 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; Niosi, 1995; Senker, 1996; Gulati, 1998). The venture capital environment of the firm, as well as its ability to tap resources from it, is considered a major growth factor of successful firms. Biotechnology firms tend to cluster in regions where venture capital is abundant. In the same direction, the capability to attract ideas from research universities and government laboratories are key factors of growth in these science-based activities (Kenney, 1986; Enright, 1998; Prevezer, 1998). Firms located in fertile regions with venture capital and good and abundant scientific institutions are more likely to grow than those in backward regions are. The institutional environment seems to play an even larger role in the national system of innovation perspective: only nations with adequate research and financial systems do really grow successful biotechnology firms (Bartholomew, 1997). Finally, biotechnology firms prosper if they are able to conduct alliances with large pharmaceutical corporations or large seed producing firms that will bring financial resources, manufacturing and marketing knowledge as well as regulatory expertise to the emerging enterprise.

A less abundant literature has examined more in detail the differential growth rate of new firms (Eisenhardt and Schoonhoven, 1990). Since the mid-sixties (Stinchcombe, 1965) authors have been aware of the liabilities of newness and smallness. Also, the literature has put emphasis on the importance of starting conditions in these new firms. These conditions include the founding team (its quality and size), the main strategic decision (product choice, markets targeted), and the environment. Too much competition among new firms appeared as a major liability.

### 3.2 A few major hypothesis

We can derive a few major hypotheses from the above discussion. They relate to both strategy and internal conditions as well as to the environment and the external conditions.

Strategic (internal) conditions of fast growth include

- H1: Targeting high-growth product niches
- H2: Targeting major (export) markets
- H3: The size and quality of the founding team
- H4: Patenting products, indicating innovative R&D
- H5: Efficient R&D management
- H6: Capacity to obtain venture capital

Environmental conditions of rapid growth include

- H7: Alliances with universities
- H8: Alliances with government laboratories
- H9: Alliances with national firms
- H10: Alliances with foreign corporations
- H11: Consumers acceptance

## 4. The Study

This study has tested some of the above-mentioned hypothesis, by building a sample of nearly thirty 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.

**Table 1: Regional distribution of companies interviewed**

Region	Total sample	Total Canada (1)
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%)
<b>Total</b>	<b>60 (100%)</b>	<b>282 (100%)</b>

(1) Statistics Canada: Canadian Biotechnology Statistics, Ottawa, 1999

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 growth of 50% and over of total employment and/or sales between 1994 and 1998; only firms having crossed the threshold of 25 employees and/or \$2 million 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 ten years old, and only six firms (10 per cent of the sample) were older than twenty-five years. The median firm had twenty-six employees and the median sales were \$0,6 million in 1998. Twenty-two companies were public (their shares being listed in the Toronto, Montreal, Alberta, Vancouver and/or NASDAQ stock exchanges), while thirty-eight of them were privately held. Among public companies, the median firm was public since 1994. Also, 90 per cent of the companies interviewed were Canadian-owned and –controlled. Out of some forty-one firms that we had designated as being rapid-growth firms, some 28 were interviewed, five refused to collaborate and eight were out of business by the time we contacted them. Similarly, out of the 40 companies without growth, some fifteen refused to collaborate, eight went bankrupt or merged, and were replaced by other slow- or no-growth firms.

As to the product areas, 55 per cent of the companies (32 firms) were in the area of human health, 28 per cent in ag-bio, 13 per cent in environment, 5 per cent in food and 12 per cent in other sectors. A few companies were active in two areas thus explaining that percentages are over 100%. This distribution closely reminds that of Statistics Canada, where 46 per cent of the firms are mainly active in human health, 22 per cent in ag-bio, 11 per cent in environment, 7 per cent in food and 14 per cent in other areas (Statistics Canada, 1999) (see Table 2).

#### 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 explaining growth was thus rejected, as a constant (R&D activity) can not explain a variable (growth rates). The median R&D personnel in 1998 was ten employees, and the median R&D expenditure was \$1 million. This R&D usually produced patents, but twenty-one companies had no patents at all, while the median was two patents per firm. Also, 39 per cent 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 among 72 per cent of those firms that exported, the United States was the major market for their exports. Western Europe was the first foreign market for 22 per cent of the exporting firms.

**Table 2: Product distribution of companies interviewed**

Area/product	Total sample	Total Canada (1)
Human health	55%	46%
Ag-bio	28%	22%
Food	7%	11%
Environment	5	7%
Other	12	14%
<b>Total</b>	<b>60 (100%)</b>	<b>282 (100%)</b>

(1) Statistics Canada: Canadian Biotechnology Statistics, Ottawa, 1999

Twenty-nine companies (48 per cent) had obtained venture capital, and the median venture capital financing obtained by the firms, usually through several rounds, was \$3.5 million. 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 and the median market capitalization by late May 1999 was \$43 million. Most of the companies (sixteen out of twenty-nine or 57 per cent) 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.

However, venture capital did not come without difficulties. Eighteen companies complained about venture capital organizations. Their complaints could be summarized under four major headings. A) Canadian venture capital organizations finance biotechnology firms by small amounts, an average of one million dollars per round. This amount was considered insufficient and new firms had either to go through several rounds of financing, or to find allies to support them at very early stages of their product development. Allies could not properly value the value of the products at a very early stage of development, and finding appropriate partners was thus difficult for firms working on Phase I or II clinical trials. In other words, according to the executives of the interviewed firms, Canadian venture capitalists spread their biotechnology investments too thin into many companies to reduce risk, but doing this they reduced the chances of any emerging company being successful. B) Canadian venture capital organizations are also supposedly more interested in financing software start-ups than biotechnology firms. Emerging software companies have shorter life cycles and venture capitalists recuperate their investment much faster than in biotechnology. Thus when dealing with biotechnology firms, venture capitalists seem either not to understand the technology or to operate with a very short-term horizon, using software firms as their benchmark. C) Several biotechnology companies complained about the long time period and efforts they had wasted in attracting attention from Canadian venture capitalists. D) Finally, some biotechnology directors complained about the lack of management advice obtained from venture capitalist organizations, while others seemed conversely to be wary of too much advice or involvement of the venture capitalists in the biotechnology firms.

Alliances are 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 per cent) conducted alliances. By far the most frequent partnerships were aimed at basic research with universities (66 per cent of the firms conducting alliances had university partners), but 30 per cent of the firms with partnerships had alliances with other companies, aiming at either R&D, manufacturing or marketing. The most common goal was research, both with university, government laboratories and other firms (90 per cent of the biotechnology firms with alliances had this type of alliance), followed by marketing (33 per cent of the firms with alliances) and manufacturing (31 per cent)<sup>1</sup>. Seventy per cent of the firms considered alliances and collaborative agreements a major growth factor. Most of them expected and obtained advantages from alliances (see Table 3).

<sup>1</sup>These percentages are all calculated on the firms conducting alliances and the question had non exclusive multiple responses.

**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%)

The differences between the advantages expected and obtained were usually related to the early stage of the alliance: the expected advantages had yet to materialize. Not unexpectedly, 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 closed the list. As to the "other advantage", the most frequent consisted in credibility. Partnerships increased the companies' credit 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: they wanted to publish, while companies preferred to keep information secret as long as possible. These difficulties affected four companies. B) Large industrial partners were usually slow, or had different priorities, or were more bureaucratic and/or did not know the technology. The latter was by far the most common complaint about alliances. It occurred in thirteen cases.

Obstacles to growth were many. Access to capital and to skilled human resources were by far the most important ones (Table 4). High-level managerial and top level scientific talent seems to be in scarce supply in Canada, and these were the skills that companies were 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 4: Obstacles to growth**

<b>Obstacles</b>	<b>All companies</b>	<b>Most important</b>
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%)
Consumers 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.

#### 4.3 Explaining fast growth

A few factors explain rapid growth. I hypothesized that both internal activities and strategies, such as the product areas, the 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 consumers' acceptance. We first correlated some key variables with the dependent one (Table 5). Then we built a logistic regression (see Table 6).

**Table 5: Correlation (Pearson)**

	Ragro	Age	Hhealth	Patent	Vencap	Alliance	Forall	Delays	Public	Consac1
Ragro	1.000									
Age	.149	1.000								
Hhealth	.242	.252	1.000							
Patent	.235	.106	.337	1.000						
Vencap	.052	.249	.223	.381	1.000					
Alliance	.330	.065	.094	.136	.114	1.000				
Forall	.185	.321	.264	.218	.061	.797	1.000			
Delays	.139	.064	.117	.043	.017	-.068	-.061	1.000		
Public	.328	.006	.410	.322	.100	.148	.182	-.171	1.000	
Consac1	.042	.354	.055	.070	.072	.092	.044	.072	.153	1.000
Export	.237	.179	.146	.088	.036	.131	.233	.003	.223	.122

Age is a main determinant. Biotechnology firms become mature only after many years of research and development, including clinical trials (in human health) and field tests in agricultural biotechnology and environment. 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 consumes usually years of mutual accommodation and learning.

Human health seems to be almost invariably the sector where rapid growth occurred. It was also the area where firms more easily obtained venture capital. Few firms outside human health had known fast growth.

Few firms could avoid having 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 their 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 consider patents strategic assets.

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 the Canadian market could experience rapid growth.

Alliances are a key determinant of growth. However, 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 as to complete their Phase III assays, or their field trials, and then organized alliances with foreign partners. Alliances thus were a necessary condition of growth only if properly managed.

**Table 6: Explaining rapid growth**

- V 1: AGE (Number of years after foundation)  
 V 5.1 HHEALTH (Products targeted for human health)  
 V 7.1 EXPORT (Company exports products, Y/N)  
 V 13.1 PATENT (Number of company patents)  
 V 14.1 VENCAP (Company obtained venture capital, Y/N)  
 V 18 ALLIANCE (Company conducts alliances, Y/N)  
 V 25.16 CONSAC1 (Consumers' acceptance is major problem for those not growing)  
 V3.6 RAGRO (Rapid growth), dependent variable

-2 Log Likelihood	51,018		
Goodness of fit	84,783		
Cox & Snell	0,307		
Nagelkerke	0,412		
	Chi-square	Df	Significance
Model	18.719	7	0,0091
Block	18.719	7	0,0091
Step	18.719	7	0,0091

Classification table for V3.6  
 The cut value is 0.50

<u>Observed</u>	<u>Predicted</u>		
	<u>Y</u>	<u>N</u>	
Growth Rapid	16	6	72,73%
Not rapid	4	25	86,21%
Overall	20	31	80,39%

Variables in the equation

Variable	B	S.E.	Wald	Df	Sig	R	Exp. (B)
V1: AGE	.0509	.0371	1.8804	1	.1703	.0000	1,0522
V5.1: HHEALTH	.9358	.7331	1.6293	1	.2018	.0000	2.5492
V7.1: EXPORT	1.4961	.9528	2.4657	1	.1164	.0817	4.4643
V13.1: PATENT	.1088	.0739	2.1660	1	.1411	.0488	.1,1149
V14.1: VENCAP	1.4614	.8197	3.1789	1	.0746	-.1300	.2319
V18: ALLIANCE	3.9976	37.1837	.0116	1	.9144	.0000	8,2303
V25.16.CONSAC1	-1.5100	1.5371	.9650	1	.3259	.0000	.2209
Constant	-4,1881	1,5712	7,1053	1	.0077		

Finally, consumers' acceptance was not a problem for firms 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, a few niches in ag-bio and food (especially nutraceuticals) were unaffected by negative consumers' receptions of their products.

Out of thirty-two firms operating in human health, nineteen of them attracted venture capital (59 per cent) and also nineteen experienced rapid growth. Most of them had alliances, including with an aim to manufacturing and marketing. Conversely out 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.

**Table 7: Rapid growth and major product areas**

Human health

	Human health		Total
	Yes	No	
Rapid growth. Yes Count	19	9	28
% with rapid growth	68%	32%	100%
% in Human health	58%	33%	47%
% of total	32%	15%	47%
No Count	14	18	32
% with rapid growth	44%	56%	100%
% in Human health	42	67%	53%
% of total	23%	30%	53%
Total count	33	27	60
% of total	55%	45%	100%

Fisher's Exact test (2 sided) significance = 0.074. One sided = 0.053

## Ag-bio

	Ag-bio		Total
	Yes	No	
Rapid growth. Yes Count	7	21	28
% with rapid growth	25%	75%	100%
% in Ag-bio	41%	49%	47%
% of total	12%	35%	47%
No Count	10	22	32
% with rapid growth	32%	69%	100%
% in ag-bio	59%	51%	53%
% of total	17%	37%	53%
Total count	17	43	60
% of total	28%	72%	100%

Fisher's Exact test (2sided) significance = 0.775; One sided = 0.403

In agricultural biotechnology, out of seventeen companies interviewed, seven experienced rapid growth (41%) and ten did not (59%). While human health companies represented 68 per cent of firms with rapid growth, agricultural biotechnology represented another 25 per cent, environment 3 per cent (one firm) and food products, basically nutraceuticals, six per cent (two firms). None of the companies operating in other product areas had experienced rapid growth.

The difficulties experienced by the environmental firms was 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 ample access to venture capital. Table 8 summarizes some relevant data about venture capital by major product area.

**Table 8: Venture capital by major product area**

Human health

	Venture capital obtained		
	Yes	No	Total
Human health. Yes Count	19	13	32
% within human health	59%	41%	100%
% with venture capital	66%	43%	54%
% of total	32%	22%	54%
No Count	10	22	32
% within human health	37%	63%	100%
% with venture capital	35%	57%	46%
% of total	17%	29%	46%
Total count	29	30	59
% of total	49%	51%	100%

Fisher's Exact test (2 sided) significance = 0.119; One sided = 0.073

## Ag-Bio

	Venture capital obtained		
	Yes	No	Total
Ag-Bio. Yes Count	6	11	17
% within Ag-Bio	35%	65%	100%
% with venture capital	21%	37%	29%
% of total	10%	19%	29%
No Count	23	19	42
% within Ag-Bio	55%	45%	100%
% with venture capital	79%	63%	71%
% of total	39%	32%	71%
Total count	29	30	59
% of total	49%	51%	100%

Fisher's Exact test (2 sided) significance = 0.252; One sided = 0.143

Table 7 shows that 59% of the human health firms had obtained venture capital, and that they represented 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 per cent of the sample's firms). In other terms, human health firms obtain more easily venture capital than any other category.

Against all expectations, some variables were not significant. Public companies did not behave much better than private ones (Pearson correlation between PUBL and RAGRO was only 0,32180). Several reasons 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 to having access to a large capitalization.

#### 4.4 Explaining rapid growth, phase II

A new logistic regression added two other variables. These were the nature of the alliance and whether the firms had experienced major delays in the development work. The new regression beats randomness by some 38 per cent, achieving almost perfect fit (see Table 9). When alliances are made with overseas partners and major delays in product development do not occur, then rapid growth has much higher chances to take place.

**Table 9: A second logistic regression on growth**

V 1: AGE (Number of years after foundation)  
 V 7.1 EXPORT (Company exports products, Y/N)  
 V 13.1 PATENT (Company has patents, Y/N)  
 V 14.1 VENCAP (Company obtained venture capital, Y/N)  
 V 19.7 FORALL (Company conducts alliances with foreign partners, Y/N)  
 V 25.16 CONSAC1 (Consumers' acceptance is major problem for those not growing)  
 V3.6 RAGRO (Rapid growth) dependent variable

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-2 Log Likelihood	29.517		
Goodness of fit	29.622		
Cox & Snell	0,484		
Nagelkerke	0,646		
	Chi-square	Df	Significance
Model	27.102	6	0,0001
Block	27.102	6	0,0001
Step	27.102	6	0,0001

Classification table for V3.6  
 The cut value is 0.50

<u>Observed Growth</u>	<u>Predicted</u>		
	<u>Y</u>	<u>N</u>	
Rapid	15	4	78.95%
Not rapid	<u>3</u>	<u>19</u>	86.36%
Overall			82.93%

---

Variables in the equation

Variable	B	S.E.	Wald	DF	Sig	R	Exp. (B)
V1: AGE	-.1589	.1124	1.9975	1	.1576	.0000	1.1722
V7.1: EXPORT	3.4605	1.4639	5.5882	1	.0181	.2517	31.8341
V13.1: PATENT	.2376	.0955	6.1942	1	.0128	.2722	1.2682
V14.1: VENCAP	-3.6421	1.5759	5.3412	1	.0208	-.2429	.0262
V19.7: FORALL	3.6939	1.5809	5.4599	1	.0195	.2472	40.2030
V25.16.CON SAC1	-4.3018	2.2104	3.7876	1	.0516	-.1777	.0135
Constant	-6.6240	2.5800	6.5917	1	.0102		

This regression improves the estimation of rapid growth, but we lose some cases due to missing responses in the new variables. Foreign alliances were associated with rapid growth. Firms with overseas partners usually tapped larger markets and thus benefited from rapid increases in sales and employment. Adding the DELAY variable to the regression also improved its fitness. Firms without delays in product development (due to wrong targeting of products, unexpected difficulties in R&D, or inefficient clinical essays) were more often first in the market and recuperated easily their investment.

Companies with slow or no growth experienced similar difficulties to those with rapid growth. One key variable, however, was access to capital, their major obstacle and the one they qualified as crucial (see Table 10). Most of these companies found themselves in a position where further, downstream obstacles, did not appear relevant, as they were trapped in their starting phase.

**Table 10: Obstacles to growth in firms with slow or no growth**

<b>Obstacles</b>	<b>Obstacle</b>	<b>Most important</b>
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%)
Consumers 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%)

## Conclusion

In the last twenty-five years, biotechnology has emerged to capitalize on the extraordinary development of molecular biology, genetics and biochemistry that took place in the Post war period. Several thousand companies across the world, including nearly 300 in Canada have created or are developing thousands of new therapeutic compounds, hundreds of 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 them will grow provided they adopted the right strategies and mix of products.

In our sample, rapid growth was associated with a certain age of the biotechnology firm, usually operating in human health products (an area without the problems of consumers' acceptance that plague both environment, food and agricultural biotechnology). Also, fast-growing enterprises adopted a strategy of patenting major novelties, looked for and obtained venture capital financing, and searched large market by exporting their products, usually through alliances with foreign corporations. Internal R&D capabilities (and probably some luck) made that they did not have major delays in delivering their products, or in moving from one phase to the next.

These findings bring some confirmation to both internal growth and competence theories of the firm, as well as the external growth perspectives. Targeting the right niche, patenting, efficient R&D and exporting are all in the area of firm strategy and are to be related to managerial competencies. However, R&D and innovation as such, because they are pervasive, are not exclusive to rapid-growth companies. Product development efficiency, though, is related with 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.

External growth theories also receive strong confirmation: access to capital, usually obtained either through venture capital 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 favour 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.

Even in a difficult financial environment, companies can improve their chances of rapid growth. The following conclusions and recommendations can be derived from this study.

1. Companies should patent their inventions as a way to signal the financial community of the novelty of their future products, thus their exclusivity. Venture capital is much easier to obtain when the companies possess patents, and venture capital is a major growth factor in biotechnology.
2. Avoiding major delays by conducting R&D on several products, not simply one, and eventually abandoning dead ends. One-product firms are usually too risky for venture capital. Mergers with other small biotechnology firms working in compatible areas can help to increase the chances of having patents, thus venture capital, augment visibility and critical mass, and obtain larger IPOs.
3. Targeting export markets: the Canadian market is too small to support any biotechnology product. 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.
4. Looking for venture capital: Venture capital provides not only cash to firms but also management and financial services, as well as credibility to the emerging firm.
5. Conducting alliances, but timing them. Alliances may procure substantial resources to emerging biotechnology companies. However, alliances are not always successful. Too early an alliance can lead to contracts were the biotechnology firms loses most of the benefits of its innovation but conversely it can help a cash-strapped firm. If the alliance comes too late the biotechnology firm may already find itself in a weak position due to cash flow problems. The best option for the biotechnology firm is to obtain venture capital, access to the capital market, and organize partnerships at the end of Phase III clinical trials or field tests, when their products are already tested and approved.

6. Planning the IPO: Going public was not a condition of rapid growth. Some of the companies that had obtained access to the stock market had only collected a few million dollars through their IPOs, while others had known major delays and product retargeting after raising substantial amounts from the financial market.

The general idea that comes out of this study is that, in a very competitive market, where hundreds of biotechnology enterprises compete for capital with other new enterprises, the emerging biotech companies should proceed through a sequence of almost unavoidable milestones. These will signal the financial community of the value of the new firm. The milestones include patenting, obtaining venture capital, and launching as early as possible their products in the overseas market, usually with the help of large foreign partners.

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