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ETLA 2004 SURVEY ON THE FINNISH BIOTECHNOLOGY INDUSTRY – Background and Descriptive Statistics

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ABSTRACT: ETLA, the Research Institute of the Finnish Economy, conducted surveys at the end of 2004 and at the beginning of 2002 on the enterprises listed in the Index of Biotechnology Companies in the Finnish Bioindustries organization. The surveys provide data on financial accounting, R&D activities, intellectual property rights, and sales forecasts. In addition to the updates, the ETLA 2004 Survey also provides detailed linkages to product-level information that incorporates R&D- and sales figures, forecasts thereof, collaboration patterns, science-base mapping, and academic origin of the innovations. This also paper presents descriptive statistics on intellectual capital and value creation of the biotechnology industry. Finally, we discuss the main findings of the survey and indicate topics for further research.

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1. Introduction

The biotechnology sector is expected to initiate a new phase of technological development that will have a pronounced impact on economic growth. ETLA has been involved in the research of managerial economics of biotechnology since the beginning of 2002. Several overviews and analyses of the Finnish biotechnology industry have been made, with most of the results of these studies presented and published by Hermans, Kulvik and Ylä-Anttila (2005) and Hermans (2004). ETLA carried out two surveys of biotechnology companies, the first in spring 2002 and the second in fall 2004. This study describes the data of the second survey.

The number of biotechnology companies grew sharply until the beginning of the millennium. At the end of 2003, there were about 120 biotechnology companies in Finland, with no significant change from 2001. Despite stagnation in growth, the Finnish companies constitute almost 7 percent of the entire number of biotechnology companies in the European Union (EU). This is a considerable amount if we compare it to Finland's population of 5 million, about 1.3 percent of the EU population in 2003. Finland can be considered a biotechnology intensive country. However, Finnish companies are limited in their size and ability to exploit their market potential: about 110 of the Finnish companies are small or medium-sized.

Most of the Finnish biotechnology business activities are connected with healthcare applications. Almost 60% of the small and medium-sized biotechnology companies are related to the pharmaceutical industry or research. The pharmaceutical markets hold high growth expectations due to the development of medical research and the ageing of the population.

However, the risks related to drug development are also high due to a particularly risky research and development (R&D) process, as well as the complex marketing in a global scheme. This induces the need for giant pharmaceutical companies to control risk through external collaboration in R&D activities. Thus, many giant pharmaceutical companies have out-sourced part of their biotechnology-based R&D activities to small research-intensive biotechnology companies.

The second ETLA survey of the Finnish biotechnology sector focuses primarily on these small- and medium-sized biotechnology enterprises (SMEs)[1]. This narrower focus is justified as the inclusion of the handful of giants active in Finland would distort and eliminate effects that the numeral majority of biotechnology companies have on the analyses[2]. Furthermore, one could assume that larger and more mature companies resemble more those in other sectors in terms of firm characteristics relatively than small and medium-sized companies due to the more consolidated state of business. Thus, the inclusion of large-sized firms might have diluted and disguised findings stemming from characteristics distinctive for biotechnology businesses.

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[1] SMEs in this paper are defined according to official definitions of the EU excluding firms with over 250 employees and match additionally at least one of the following criteria: (i) Annual turnover > 50 mill. EUR, (ii) balance sheet total > 43 mill. EUR.

[2] Orion Pharma alone, for example, has publicly disclosed it has over 2400 employees in Finland compared to the total employment of all Finnish biotechnology SMEs of about 2500.

This paper deals with the Finnish biotechnology industry and is organized as follows: After the introduction, Section 2 gives an overview on the conclusions made from the preceding ETLA 2002 survey published in or submitted to international scientific journals. Section 3 presents some descriptive statistics on the ETLA 2004 survey through three complementary approaches. The first approach deals with intellectual capital, the second with financial sources, and the third with regional context. Finally, Section 4 concludes and makes suggestions for further research.

2. Overview of the ETLA 2002 survey with Policy Implications

2.1 ETLA Survey 2002 data

The first ETLA survey on the Finnish biotechnology industry was performed in March-May 2002 by ETLA and Etlatieto Ltd and first reported by Hermans and Luukkonen (2002). The survey was carried out through telephone interviews. There were 116 firms in the population, which was obtained from the Finnish Bioindustries Association. Eighty-four firms replied, equaling a response rate of 72 percent. Despite the high response rate, the sample was partially skewed towards matured companies. There were proportionally fewer infant firms, founded 1997-2001, in the sample than firms in other age groups.

2.2 Recent Economic Research related to the ETLA 2002 survey

There are several articles that have been published in or submitted to international scientific journals based on the preceding ETLA survey. These articles deal with themes in the field of the managerial economics of biotechnology. Each of the articles contains policy implications for both the industry and the public sector.

2.2.1 Economic Integration and Regional Competitiveness

The biotechnology industry cannot be treated as a sector of its own, isolated from the mega-trends affecting international economic development. Hermans (2005) investigates the effects of economic integration on the regional location of production in-line with the body of the international trade literature known as the new economic geography theory.

The main idea of the study is to compare the differences between countries' internal regional structures on the one hand, and international regional structures, on the other. Economic integration can be assumed to be deeper within countries than internationally. For decades the trade has been free within European countries and there has been a cultural unity between different regions within the same country. This situation can be considered an extreme economic integration. At the same time, there are certain trade barriers between countries including tariffs or quotas, as well as cultural differences and respective geographic locations. In recent years the economic integration has, nevertheless, deepened in Europe as well as globally.

One of the main findings of Hermans (2005) is that economic activity tends to become agglomerated on regions where the innovation intensity is higher than in other regions. Such a linkage between spatial agglomeration and innovation intensity could not be found between countries. However, if the international integration deepens, as it has domestically by a lowering of trade barriers and cultural differences between regions, then by investigating the countries' domestic regional structures we can predict and evaluate the trends in the integrating international economies.

Hermans (2005) predicts that at the international level economic activities will become agglomerated in regions where there is a high intensity of investment in innovative activity. This scenario brings challenges also for Finland, which is located geographically on the periphery of Europe.

The new economic geography framework enables us to make policy recommendations of a general nature. Fostering a high intensity of innovative activity, for instance, is a central way of attracting direct investment and keeping jobs in the region. In order to deepen the policy recommendations it is fruitful to look at the theoretical framework of Ricardo as well as Heckscher, Ohlin and Samuelson (HOS), which are based on comparative advantage. According to the HOS framework, free trade leads to regional specialization of production in goods requiring resources (knowledge, capital, natural resources) that are relatively abundant in the region. Nelson (1990) also emphasizes the significance of comparative advantages generated by natural resources and intellectual capital facilitating the functioning of the national innovation system. Taking advantage of the principle of comparative advantage at the international level is deemed to increase the welfare of all the countries participating in free trade.

2.2.2 Market Structure of the Pharmaceutical Industry

The pharmaceutical industry is one of the main sectors that have been able to take advantage of biotechnology in its product development. It is thus important to evaluate the market structure of the pharmaceutical industry in order to be able to conceptualize the playground, on which also most of the Finnish biotechnology companies will at least in part operate.

Hermans and Linnosmaa (2005) compare the price cost margins of the pharmaceutical industry prevailing in Finland and the United States in 1975-1999. The study is based on the same theoretical framework as Linnosmaa, Hermans and Hallinen (2004). The effects of research and development costs have been added to the model.

The development of drugs is heavily regulated by the public sector in both Finland and the United States via the mandatory procedures for getting new drugs approved. The pharmaceutical market in Finland has been marked by extensive price regulation while price setting in the US has been free (Rinta 2001). Most of the pharmaceutical industries' products in both countries have ended up meeting domestic demand during the period under investigation. It could be imagined that the domination of markets by domestic manufacturers and differences in price controls would mean that the price-cost margins of the Finnish pharmaceutical industry would remain at a lower level than in the US. In other words, we can assume that Finnish companies have less price setting power than US companies.

A main finding of Hermans and Linnosmaa (2005) was that no difference between Finland and the United States in the average price-cost margins of the pharmaceutical industry could be found during the period under investigation. This result is surprising given the fundamental difference in price controls in the respective two countries.

On one hand, this phenomenon may stem from the dual nature of the pharmaceutical markets in both countries. Drugs protected by patents or brand name products can be priced at a higher level in the United States in line with monopolist principles. In Finland, on the other hand, patent-protected products have been subject to price controls. In the United States, after the expiration of patent protection, there are huge markets for generic drugs and competition is fierce, which pushes down the level of prices.

There has been a process patenting system (sentence incomplete) In Finland, competition with respect to generic products has not been as keen owing to the relatively small market potential and the tendency of domestic manufacturers to turn their products into brand names. The above-described differences between the market structures of these two countries and the segmentation of markets between patent-protected and generic products may lead to the same average overall price-cost margins in the pharmaceutical industry.

It is also possible that the Finnish price control system has not worked in the way desired, in the sense that the pharmaceutical companies have been able to negotiate a relatively high price level for their drugs. Deeper analysis of the market structure and regulatory schemes is necessary so that we can shed light on the reasons behind the similarities in the market power of the pharmaceutical industry.

The historical development of the drug industry, its present competitive situation, as well as price setting behavior, are of great significance for the biotechnology industry. Owing to the considerable costs and risks associated with drug development, large pharmaceutical manufacturers have begun to outsource the initial stages of their research and development activities to smaller biotechnology companies.

2.2.3 Academic spin-offs in Biotechnology

Tahvanainen (2004) describes the characteristics of Finnish biotechnology SMEs that have their origin in academic research conducted in universities or other comparable research institutions. The description facilitates the positioning of these firms within the sector as a whole and, even more importantly, enables the identification of strengths and weaknesses of academic biotechnology spin-offs, as well as external factors that either promote or inhibit their prosperity from an entrepreneurial perspective.

Leaning on results of a linear regression analysis based on a sample of 65 companies, it is found that academic biotechnology spin-offs are constraint in several ways. First, they lack a clear market-oriented focus, as well as the commercial sense and skills to strategically direct their organization as a business towards the markets. They are technology-focused. This is apparent in that there is often no existing business plan, cooperation activities are relatively poor, firms rely heavily on lead-time to protect their innovations, and do not utilize alternative business modes – e.g., offering services or acquiring licenses to products – to generate initial revenue that would make them less dependent on financial markets from the beginning of operations.

One could think that business expertise can be recruited from outside the industry itself. In other European countries, managers have been recruited from, for example, the traditional pharmaceutical industry. Venture capitalists with biotechnology business specific expertise have also brought business skills into their portfolio companies. Finland is faced with the problem that does not have a long industrial history in the development of pharmaceuticals or any other branch of industry that requires expertise comparable to that needed in the biotechnology business. A large pool of skilled individuals with relevant background from which to recruit is simply non-existent in Finland.

Second, a very traditional and detached perception and definition of the academia's role and task within society – the concept of the "ivory tower" – as well as high in-come tax regimes in Finland make it difficult for the academic entrepreneur to attract skilled labor, the most important resource in R&D-intensive industries. And last, with only one true seed stage risk capital provider, Sitra, Finland's equity markets are underdeveloped. With a full portfolio of companies, that Sitra is currently unable to exit from at, new seed capital is almost unavailable, as private and foreign VCs invest only in companies that are already very close to the markets and have established a viable business.

For the situation to improve, measures have to be designed and applied actively not only at the firm but also at the national level. At the firm level, the greatest challenge is to switch from a technology-driven mode towards a strongly market-oriented mode. This calls for educational services focusing on processes of commercialization, strategic thinking, project and technology management, as well as the role of immaterial property rights and the importance of cooperation. At the national level, the definitions of the role and task of the academia require expansion aiming at the disintegration of the "ivory tower" in order to free academics from a purely science- and technology-focused view of the world.

2.2.4 Sources of Financing of the Finnish Bio-Pharmaceutical Industry

Drug development is heavily regulated in the industrialized countries. The drugs have to go through pre-clinical tests on animals and clinical tests on people, a process that ordinarily takes several years. The tests are designed to assess the suitability of the drug molecules for humans as well as the desired effects on a certain sickness or alleviation of symptoms. Depending on the type of medication, the number of people to be tested may climb into the hundreds or even thousands. The third stage of clinical tests, in particular, costs vast sums of money.

The international marketing of pharmaceuticals is very expensive and even large-scale marketing efforts cannot guarantee a product breakthrough. Many new drugs are marketed directly to the physicians who write the prescriptions. On the other hand, the promotion of prescription medication is to a growing extent also directed toward the final consumers.

As the innovation activity of large international pharmaceutical companies is unable to produce enough new commercially successful products, large pharmaceutical companies have decided to outsource their R&D activities and risks to small biotechnology companies. Large pharmaceutical companies can help bring the most promising innovations of small biotechnology companies to the market. In practice, the large companies can buy licenses, all of the rights, or a majority or minority stake in the companies that undertook the development work.

According to Hermans (2003, 2004b), the transfer of prolonged promising projects to another pharmaceutical company is reflected in the ownership structure of Finnish bio-pharmaceutical companies. The older companies generating sales revenues have a different ownership structure than the younger ones. The owners of the older companies are mostly other companies. The ownership of the younger companies, on the other hand, is rather evenly distributed among those actively engaged in the company, Sitra[3], and private capital venture firms.

2.2.5 Measuring Intellectual Capital among Distinctive Owner Groups

The growth opportunities of small and medium-sized bio-pharmaceutical companies often lie in the distant future, and thus they are in need of external finance to reach the market. The valuation of this kind of a knowledge-intensive company can be expected to be based not only on historic earnings data, but also on intellectual capital indicating the future earning prospects of the company.

Hermans and Kulvik (2004) processed survey data in three steps in order to analyze the linkages between intellectual capital and ownership structure of the biotechnology companies. First, the sources of equity financing were identified, yielding five distinct groups of owners. Second, they formed several indicators for sub-categories of IC and constructed IC components based on the value platform framework, which combines the three categories of intellectual capital. Third, they identified how IC components were related to the equity financing of the distinct groups of owners.

The financing received from the company's investors is usually equity financing and to a lesser extent capital loans, judicially on equity terms. Conventional loan financing is not a main form of financing in the bio-pharmaceutical sector. An exit is critical particularly for an early stage investor. In the current situation prevailing in the financial markets, obtaining a listing on the stock exchange does not seem a realistic option. The licensing and royalty payments, as well as mergers and acquisitions, are the most common ways of securing consecutive rounds of financing for commercialization projects. This study setup was not designed to identify dynamic aspects in the investment patterns. However, reverting to a principal component analysis revealed combinations of variables that were able to distinguish patterns of equity financing preferences.

According to the value platform theory the interaction of the three categories of IC predicts the value creation ability of the company. This is emphasized in the bio-pharmaceutical sector as the value creation is typically expected to be fully realized far in the future, thus closely strongly suggesting the use of the value platform approach. We were able to identify three principal components that included all three categories of intellectual capital. The principal component scores for each factor were derived, enabling a creation of IC profiles for the companies.

The IC profiles derived were able to diversify between investment preferences of different owner groups. **Other firms** possess equity in bio-pharmaceutical companies with two different profiles of intellectual capital. This probably reflects two different sub-

[3] The Finnish National Fund for Research and Development (Sitra) is a public foundation under the supervision of the Finnish Parliament.

groups of companies, corresponding to different strategic functions designated to the company by the owner firm. **Venture capital companies** represented the largest investor group. They seem to prefer a well-balanced combination of intellectual capital, even more than other owner groups. **Individual owners**, **governmental venture capital institutions** and **other investors** showed among themselves a rather similar pattern of investment preferences. The role of **individual owners** and **governmental venture capital institutions** is emphasized in the early stages of a bio-pharmaceutical company's life cycle. These investor groups have directed funds to companies whose corresponding intellectual capital profiles indicate that all IC categories are not fully balanced.

2.2.6 Financial Pecking Order and Intellectual Capital

Tahvanainen and Hermans (2005) set out to answer the question whether the intellectual capital base of a company affects its capital structure. In the first stage, Tahvanainen and Hermans (2005) resorted to a factor analysis as a method to categorize companies according to their intellectual capital configurations providing every observation with a factor score for each generated factor. Then in a second stage, the factor scores were used to estimate a number of capital structure ratios derived from the capital structure literature.

The study shows for the first time that companies with differing intellectual capital bases indeed also exhibit differing capital structures. While companies with well-balanced intellectual capital bases have relatively high retained earnings and debt ratios, companies with only structural capital display relatively high capital loan ratios. Companies whose IC bases consist of human and relational capital only, show relatively high external equity ratios. In a static framework one can argue that the findings are in line with the financial pecking order hypothesis of Myers (1984), implying that, despite existing knowledge management metrics deliberately created for the measurement of IC, an information asymmetry concerning the IC of companies still persists between sample firms and financial markets.

Due to the lack of time series data, we were unable to control for a possible reverse causality of results. The dynamic development of the IC base and the capital structure of a company could well be induced by either or both with the direction of effect shifting in the course of a company's life cycle. The unveiling of a dynamic interaction between intellectual capital and capital structures constitutes an attractive area for further research that has a large potential to contribute decisively to the understanding of corporate financial behavior from the perspective of knowledge management. Injecting new interdisciplinary ideas for approaching the matter seems welcome, since the related discussion has followed rather rigid trajectories for the past two decades building incremental additions to existing frameworks (For a comprehensive review of capital structure theories and their development over time see, e.g., Harris and Raviv 1991). Tahvanainen and Hermans (2005) point out the necessity of using time series data if such research is conducted.

As a policy implication Tahvanainen and Hermans (2005) suggest that IC metrics should be applied in investment decisions. IC metrics could be compared between an individual firm and the entire industry. It seems that IC metrics could stand as a basis for the evaluation of the most promising investment decisions and as a basis for a strategically meaningful development of companies after the investment decision.

2.2.7 Intellectual Capital and Value Creation Potential in Biotechnology

The present value of a company is based on the expectations of its future returns. The historical accounting data for the biotechnology industry does not enable us to form expectations based on previous revenue and profitability figures. When making investments, external investors should have indicators at hand that help them project future earnings in light of the company's current situation. Without such measures, the earning expectations with respect to the potential investment target may be distorted.

According to the literature related to knowledge management, intangible assets and intellectual capital inherently reflect a company's potential to create value and future earning expectations. Hermans and Kauranen (2005) investigate whether the growth expectations of Finnish small and medium-sized biotechnology companies are attributable to their intangible assets. Their objective is to empirically verify impacts of intellectual capital on the anticipated future sales of companies.

In the study the value of a company's intangible assets is quantified and defined by modeling the intellectual capital and value creation of companies from the viewpoint of knowledge management. The model is able to explain about 70% of the biotechnology companies' anticipated sales in 2006. Technically, the model's ability to explain 70% of the variance of the anticipated future sales controls for the risk of randomness of these anticipations disclosed by the biotechnology companies. This means that a large portion of the companies' growth expectations is based on the value stemming from intangible assets. This approach also offers a means for making economic projections based on the companies' growth expectations.

It seems that a well-balanced combination of human capital, structural capital, and relational capital implies value creation potential and high- anticipated future sales. This notion calls for a well-prepared strategy even for the early stages of the company so as to attract capital inflows. Despite many companies involved in drug development having high growth anticipations, there are many other promising, albeit occasionally underresourced, branches within the biotechnology industry. These include applications related to biomaterials, diagnostics, food and feed, industrial enzymes, agriculture, and forestry.

2.2.8 Growth Forecast of the Biotechnology Industry

Hermans and Kulvik (2005) compiles an economic growth forecast where the probability distribution is formed from the companies' sales growth forecast and their current sales revenues. The model also incorporates the bankruptcy risk. The modeling technique is based on the sectoral input-output method utilizing the purchase and sales volumes announced by companies in the respective sectors.

According to the forecast model based on the data from 2001 the biotechnology cluster is able to produce EUR 850-1200 million worth of value added with a probability of 90 % in 2006. In 2001, the entire biotechnology sector's value added was about EUR 500 million, meaning that annual growth of the entire cluster would be approx. 10-18 percent. Despite this, the value added will remain relatively low because the biotechnology companies use very much funds for purchasing services and goods from outside

the firm. According to the forecasting model, by 2006 the biotechnology cluster's contribution to annual GDP growth will be about 0.05-0.09 percentage points.

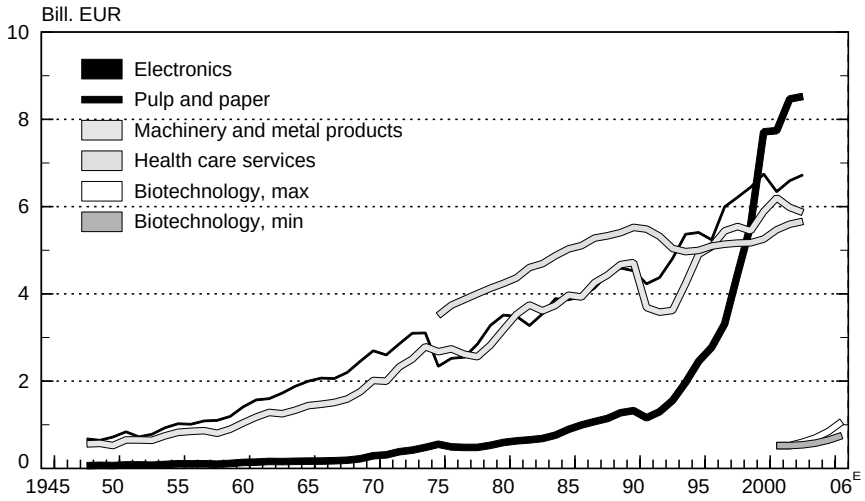

Figure 2.8 Production by sector 1970-2002, in 2000 prices (Hermans and Kulvik 2005).

Industrial history shows us that if a region or a country has no previous industrial traditions in a certain sector, successful businesses and new growth emerge slowly or only seldom. Finland has pinned high hopes on biotechnology as a source of new research-intensive growth. Almost all industrialized countries have the same goal, and many of them already have relatively long traditions in this sector. The biotechnology sector has a short history in Finland. In order to put the possible growth of the biotechnology sector in perspective, we can ask when Finland's currently strong sectors – the forest, machinery and electronics industries – were in the same situation (Figure 2.8).

In 2000 prices, the value of forest industry production was half a billion euros in the early 1950s. The electronics industry reached that level in the mid-1970s. If the biotechnology sector achieved the same growth as that of the electronics industry fueled by Nokia, it would reach the position of the "fourth pillar" of industry in about 30 years. If the life cycle of the biotechnology industry as an independent sector were comparable to the forest industry, it would take 50 years. If a long run growth rate of production of the biotechnology sector is sustained at the same level as in the forecast period 2001-2006, it would take 15-30 years to reach the same production level as electronics or pulp and paper industry have today.

The healthcare sector's domestic service production is at relatively high level compared even with highly export-oriented industries (Figure 2.8). The massive healthcare sector has reached a major crossroads owing to the aging of the population and advances made in medical science. On the one hand, the aging of the population and the medical possibilities to diagnose and treat more illnesses than before increase the cost pressures on healthcare. On the other, biotechnology applications are expected to spawn cost savings over the long run by, for example, making time-consuming diagnostic methods more efficient and facilitating targeted therapy.

3. Descriptive Statistics of the ETLA Survey of 2004

3.1 The ETLA Survey 2004

The empirical evidence of the present ETLA survey is based on new data collected via a telephone questionnaire in the late fall of 2004. It is supplemented by financial statement data from The National Board of Patents and Registration (NBPR). All data describing the current state of the companies represent 2003 figures. In some individual cases financial statement data from NBPR originates from periods before 2003 as 2003 statements were not submitted to NBPR by all the sample companies. However, no data from NBPR is used that originates from periods before 2001.

3.1.1 Sample and population

The survey covers the majority of companies operating in the Finnish biotechnology sector. As the survey focuses on dedicated biotechnology companies, cluster companies specializing solely on distribution, import, consulting, and other support functions are excluded from the survey. Our sample includes 87 out of 123 active biotechnology companies in fall 2004, and 79 out of these 87 are small or medium-sized. The total population of SMEs is 111. These numbers translate into a response rate of 71% with respect to both total- and SME populations. Reasons for not obtaining data covering the complete population include denial of response, incoherent data and the non-existence of an exhaustive list of companies active in the sector at the time of survey implementation[4]. Although firms of all ages are represented by the sample fairly evenly, firms of very young age, on one hand, and those of very old age on the other are slightly better represented than those of an adolescent or middle age. Concerning NBPR data on financial statements it has to be pointed out that the sample is almost identical to the total population as financial statements could be retrieved from 117 companies (95%). Analyses based on this data are therefore highly representative.

The companies in the final sample are independent businesses, partnerships or subsidiaries of bigger corporations. In the latter two cases the businesses had to be independently responsible business units in order to be included in the sample. If the criteria were not fulfilled, the data was collected from the parent company.

3.1.2 Data

The survey covers a variety of topics, ranging from the basic characteristics of companies, over the conduct of R&D to sources financing and sales, as well as collaboration patterns and purchasing. In this respect, the survey updates the data collected in the first ETLA survey of 2001.

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[4] In fall 2004 the Finnish Bioindustries Association Index went through an update process, during which the definite number of companies active in the Finnish Biotechnology sector could not be determined. Our sample of 123 firms is based on the Index as valid in September 2004, but includes additional firms tracked down from a variety of sources.

However, the current survey is more profound in the sense that it features the aforementioned aspects in more depth. New insights include geographical and inter-institutional R&D-collaboration patterns, mapping of the academic science base on which the firms build their own R&D, detailed, comprehensive, and reliable financial statements, and, probably most importantly, product-level data that incorporates R&D- and sales figures, forecasts thereof, collaboration patterns, product-specific science-base mapping, and academic origin of the innovations. Through these new features the data allows a more thorough and detailed analysis of the sector than could have been carried out before.

3.2 Intellectual Capital in small biotechnology business

We base the measurement of intellectual capital (IC) in the sample companies on the principles presented by Edvinsson and Malone (1997). The names for the three components of IC, namely **human**, **structural**, and **relational capital**, have been modified to match the definitions proposed by the MERITUM project (2002) (see also Sveiby 1997 and Edvinsson and Malone 1997). Edvinsson and Malone (1997) talk about "customer capital" instead of relational capital, disregarding thereby relationships to all other stakeholders like suppliers, competitors, and academia. However, the latter are critical for advancing research towards the market place, as successful R&D-activities often are conducted within networks of co-operation (see, e.g. Hermans and Luukkonen 2002 or Nilsson 2001).

According to the value platform model (Edvinsson and Malone 1997), value is created in a company when all three components of IC interact with each other. While **human capital** encompasses the knowledge, experiences, skills, and competencies of the personnel, **structural capital** comprises physical and conceptual structures present in the company that facilitate the support, enhancement, protection, intra-firm distribution, and documentation of human capital residing in the company. **Relational capital** can be understood as a network of virtual and physical relationships and connections among the critical stakeholders of a company. Through this network the company is able to leverage intra-organizational achievements, be it products, intellectual property rights, services, results of research, communication, or people to the periphery of the company. According to the model, all three components are critical success factors in the sense that in the absence of any single component only modest value can be created.

3.2.1 Human Capital

As knowledge in its natural, uncodified, and tacit form resides within individuals, we utilize the total number of personnel to capture and quantify the total mass of knowledge inherent in the companies. As the biotechnology industry is knowledge-intensive in character and depends on human capital as the engine of innovation, we assume that a critical mass of complementary and cohesive human capital is essential for exceptionally high performance, or taken to the extremes, for survival.

Table 3.2.1 Descriptive statistics of human capital related variables of the Finnish biotechnology SMEs

small and medium-sized enterprises: **1**

	N	Sum	Mean	Median	Std. Deviation
Personnel	100	2450	24.5	10	41.34
Number of personnel holding doctoral degree	75	273	3.6	2	5.49
Doctors per personnel	75		30.9%	22.2%	29.5%
CEO's business experience (years)	76	919	12.1	10	8.74
Full-time marketing expertise (no=0; yes=1)	78	52	0.67	1	0.47
Full-time production process expertise (no=0; yes=1)	79	40	0.51	1	0.50

A typical Finnish small biotechnology company has 10 employees of which one in five holds a doctoral degree. The company's chief executive officer has 10 years of experience in business life and some of the company's personnel possess marketing expertise.

3.2.2 Structural Capital

Structural capital includes the way of organizing the company's activities and the intellectual property rights of the company. The structural capital of a company includes activities, schemes, policies, and programs, as well as systems, regulations, guides, rights, and facilities that support, enhance, protect, distribute, and document the human capital residing in that company. In more concrete terms this includes the organization of activities like R&D, the protection of R&D investments with immaterial property rights, company policies on diverse aspects like secrecy and competing activities, information systems and guidelines concerning the standards of conduct in the laboratory, as well as bonus and educational programs.

Table 3.2.2 Descriptive statistics of structural capital related variables of the Finnish biotechnology SMEs

small and medium-sized enterprises: **1**

	N	Sum	Mean	Median	Std. Deviation
Age (years)	79	869	11	7	15.28
Number of patents and patent applications	76	640	8.41	4	14.02
Number of patents and patent applications per personnel	76	83.9	1.10	0.32	2.63
Patent applications per sum of patent applications and patents	56	28.5	0.51	0.50	0.35
R&D expenditures (euros)	81	71,076,842	877,492	180,000	1,454,796
R&D expenditures per personnel (euros)	79	4,262,708	53,958	18,143	147,793

The typical Finnish biotechnology company was founded 7 years ago. R&D expenditures of the company are 180,000 euros annually. Due to the intensive R&D activities, its patent portfolio contains 4 patents or patent applications, of which about half are officially accepted.

3.2.3 Relational Capital

Edvinsson and Malone (1997) and Stewart (1997) define the company's relational capital as customer capital. Sveiby (1997) also takes into account supplier networks in relational structures. Market potential and catering to customer needs are fundamental requirements for success in any business. Most of the future of the market potential in small open economies results from the anticipated sales in international markets.

When speaking of the early-stage biotechnology companies, a pre-requisite in the field of relational capital is research and development collaboration and investor networks. A strong science base is necessary in order to attract large investments. (Darby and Zucker 2002.)

Table 3.2.3 Descriptive statistics of relational capital related variables of the Finnish biotechnology SMEs

small and medium-sized enterprises: **1**

	N	Sum	Mean	Median	Std. Deviation
R&D collaboration with own group	79	13	16.5 %	0	37.3 %
R&D collaboration with other companies	79	64	81.0 %	1	39.5 %
R&D collaboration with clinical units	78	28	35.9 %	0	48.3 %
R&D collaboration with universities	78	65	83.3 %	1	37.5 %
R&D collaboration with research institutions	78	47	60.3 %	1	49.3 %
R&D collaboration with others	78	9	11.5 %	0	32.2 %
Governmental financing obtained	79	76	96.2 %	1	19.2 %
Sales to a principal customer over 33% of total sales	78	34	43.6 %	0	49.9 %
Purchases from a principal subcontractor over 33%	77	17	22.1 %	0	41.7 %

The typical small Finnish biotechnology company collaborates with universities, research institutions and other companies. It has also obtained governmental financing. Most of the companies in drug development and diagnostics collaborate with clinical units.

Almost half of the companies have a principal customer (≥ 33 percent of the company's sales). Over one-fifth of the companies have a principal subcontractor, from whom they purchase over 33 percent of their input for its research and development activities and production activities.

3.3 Biotechnologies and the Fields of Applications

Throughout our survey we have used the OECD guideline for the statistical definitions of biotechnology and its subgroups (OECD 2005). Table 3.3 shows the indicative but not exhaustive list of biotechnologies.

Table 3.3. The indicative, not exhaustive list of biotechnologies as presented by OECD (OECD 2005)

DNA (the coding)	genomics pharmaco-genetics gene probes DNA sequencing/synthesis/amplification genetic engineering
Proteins and molecules (the functional blocks)	protein/peptide sequencing/synthesis lipid/protein glyco-engineering proteomics hormones and growth factors cell receptors/signaling/pheromones
Cell and tissue culture and engineering	cell/tissue culture tissue engineering hybridization cellular fusion vaccine/immune stimulants embryo manipulation
Process biotechnologies	bioreactors fermentation bioprocessing bioleaching biopulping biobleaching biodesulphurization bioremediation biofiltration
Sub-cellular organisms	gene therapy viral vectors
Other	*not specified*

The definitions are not mutually exclusive, and the groups with their subclasses are not easily intercomparable. For example, "DNA (the coding)" has as a subgroup "genomics". Genomics has been defined as "Generation of information about living things by systematic approaches that can be performed on an industrial scale" (Brent 2000), which includes a wide array of technologies and research fields. The Medical Subject Headings (MeSH) defines genomics as "The systematic study of the complete DNA sequence (GENOME) of organisms", and puts proteomics ("The systematic study of the complete complement of proteins (PROTEOME) of organisms") as a subgroup to genomics (MeSH 2001; MeSH 2003).

Proteomics again is defined as "…not only the identification and quantification of proteins, but also the determination of their localization, modifications, interactions, activivities, and, ultimately, their function. … The explosive growth of this field is driven by multiple forces –genomics and its revelation of more and more new proteins; powerful protein technologies, such as newly developed mass spectrometry approaches, global [yeast] two-hybrid techniques, and spin-offs from DNA arrays; and innovative computational tools and methods to process, analyze, and interpret prodigious amounts of data." (Fields 2001). Thus, within DNA (the coding) we have moved to the sub-areas of proteins and molecules, further to cell and tissue culture and engineering, and back to DNA (the coding).

The terms red, white, and green biotechnology are widely used to differentiate between the different application areas of biotechnology. However, the terms are in part diffuse owing to the generic nature of biotechnological techniques. Especially in the field of plant technology, the application areas and the techniques have been interchanged and used without clear definition (CGIAR 1998; ACP-EU 2003). When not stated differently, we use definitions according to EuropaBio:

The broad definition of [green] biotechnology covers many of the tools and techniques that are commonplace in agriculture and food production. Interpreted in a narrow sense, which considers only new DNA techniques, molecular biology and reproductive technological applications, the definition covers a range of different technologies such as gene manipulation and gene transfer, DNA typing and cloning of plants and animals. The development of genetically modified organisms (GMOs) should be regarded as only one application of plant biotechnology, even though it has become the focus of a heated debate where morality and money have been opposed (Biotechnology 2000; ACP-EU 2003). The aim of **Green** or **plant biotechnology** is to achieve crop improvement and production of novel products in plants. As of today, green biotechnology can be regarded as encompassing three major areas: plant tissue culture, plant genetic engineering, and plant molecular marker assisted breeding.

Plant tissue culture allows whole plants to be produced from minute amounts of plant parts such as roots, leaves or stems or even just a single plant cell under laboratory conditions. An advantage of tissue culture is rapid production of clean plant materials.

Plant genetic engineering encompasses selective, deliberate transfer of beneficial gene(s) from one organism to another to create new improved crops, animals, or materials. Examples of genetically engineered crops include cotton, maize, sweet potato, and soybeans.

Plant molecular marker assisted breeding is a technique that uses molecular markers to select for a particular trait of interest, such as yield. A molecular marker is a short sequence of DNA that is tightly linked to the desirable trait (such as disease resistance) that selection for its presence ends up selecting for the desirable trait. An example is maize that is tolerant to drought and maize streak virus.

(EuropaBio 2005)

The term **white biotechnology** encompasses an emerging field within modern biotechnology that serves industry. It uses living cells like moulds, yeasts, or bacteria, as well as enzymes to produce goods and services. Living cells can be used as they are, or they can be improved to work as "cell factories" to produce enzymes for industry. Living cells can also be used to make antibiotics, vitamins, vaccines, and proteins for medical use. Examples of applications are:

Eco-efficient enzymes which can serve as alternatives to some chemical processes to make products. Enzymes offer a biological route and often cleaner solution for industry; eco-efficient, enzymes consume less water, raw materials, and energy. The environmental impact can be minimized, yet offering better products at lower cost. For example, using enzymes in washing powder allows difficult stains to be removed at lower temperatures, saving energy and reducing the impact on the environment.

Biomass like starch, cellulose, vegetable oils, and agricultural waste are used to produce chemicals, biodegradable plastics, pesticides, new fibers, and biofuels among other

things. The processes manufacturing them use enzymes, and biomass is by definition made from renewable raw materials.

An example is ethanol, a renewable fuel made out of biomass. It has the potential to replace fossil fuels, which would have a neutral impact on greenhouse gas emissions, and could contribute to reducing global warming.

(EuropaBio 2005; Söderlund 2005)

Healthcare Biotechnology is increasingly playing a role in conventional drug discovery. Additionally, there are hopes for healthcare, or red, biotechnology to open up new possibilities to prevent, treat and cure so far incurable diseases using novel methods of treatment and diagnosis. Biotech medicines such as proteins, antibodies, and enzymes now account for 20% of all marketed medicines and 50% of those in clinical trials. Biotechnology is also increasing the number of disease targets for conventional drug therapy. Today conventional drugs target fewer than 500 disease targets, but in the future this is likely to rise to between 5-10 000 targets.

Through genetic engineering, biotechnology also uses other living organisms – plant and animal cells, viruses, and yeasts - to assist in the large-scale production of medicines for human use (bio manufacturing)

The healthcare areas in which biotechnology is currently being used include medicines, vaccines, diagnostics and emerging cell and gene therapies. The aim is to create both comprehensive and highly individualized medicines, as well as move from treatment towards disease prevention and cure. Europabio classifies the following categories as belonging to red biotech:

- Cell and tissues
- Stem cells
- Gene therapy
- Orphan drugs and rare diseases
- Proteomics
- Pharmacogenetics
- Diagnostics
- Genetic testing

(EuropaBio 2005)

We have included a short description of application for each technology in Appendix 1, as presented by EuropaBio

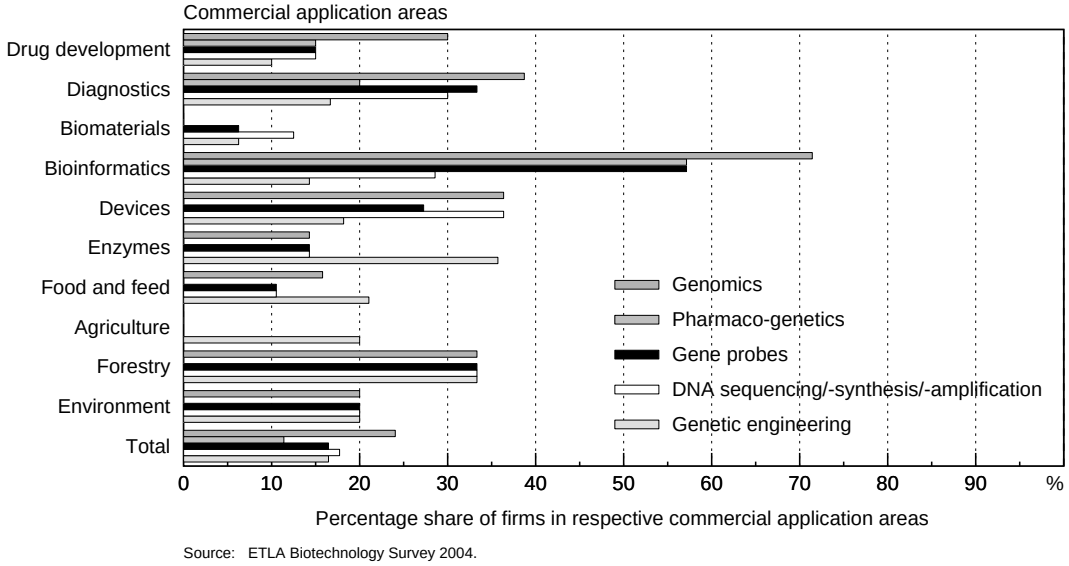
In conclusion, most of the groups are closely intertwined, and the different categories can benefit from more or less common basic technologies. This also suggests that the nomenclature in the field of biotechnology is somewhat unstructured, which according to our survey can cause confusion even among biotechnologists themselves. The intricate definitions also increase the risk of information asymmetry between different parties in biotechnology.

In the following section we use the nomenclature suggested by OECD, and look at how each technology is utilized by companies in respective areas of application.

3.3.1 DNA (the coding)

DNA not only forms the core of life, but also the core of modern biotechnology. The majority of modern biotechnological applications are based on knowledge and technologies derived from studies concerning DNA. This is reflected in the results showing that techniques classified under DNA (the coding) are used in abundance within all commercial application areas.

Especially after the development of techniques such as microarrays and the polymerase chain reaction (PCR), the amount of extracted information has grown exponentially. **Bioinformatics** is involved in the processing of this data towards meaningful applications. It seems also intuitive that diagnostics and modern drug development as well as **devices** utilize or are closely connected to DNA techniques; many diagnostic applications are based on the direct detection of DNA or RNA strands. The preponderance among forestry applications in our data is explained by the analytical strength offered by the DNA techniques; studying the genotype offers significant time savings as compared to studying the phenotypes.

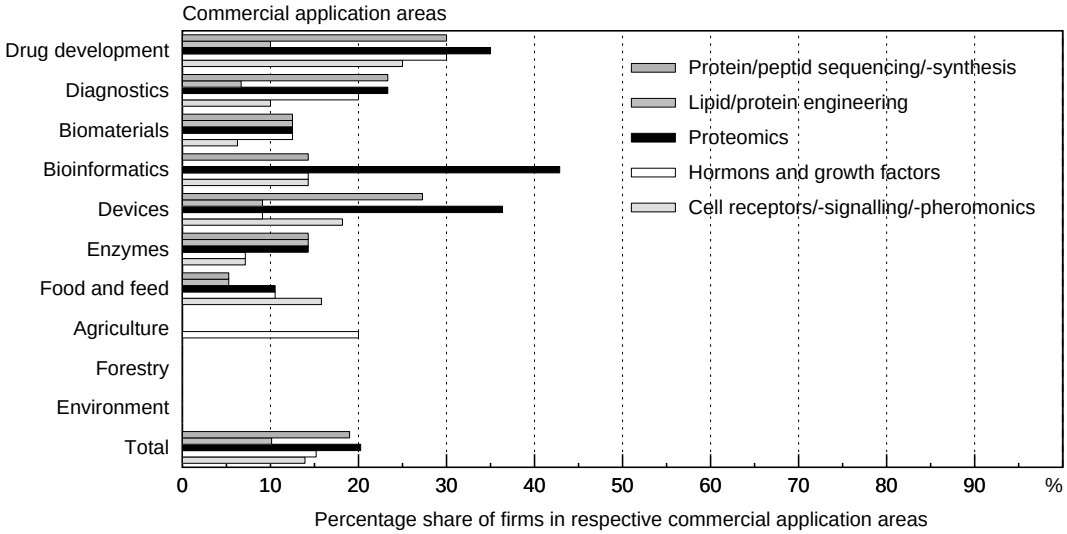


Source: ETLA Biotechnology Survey 2004.

Figure 3.3.1. Commercial application areas and biotechnologies related to the DNA coding.

3.3.2 Proteins and molecules (the functional blocks)

Proteins and molecules are constructed in a living cell according to information extracted from the DNA/RNA codes. **Proteomics** and glycomics are regarded as the following steps in the cascade of genetic information, exhibiting a strongly increasing complexity, and requiring a wide array of assay tools (Hirabayashi and Kasai 2000; Fields 2001). **Lipid/protein engineering** and proteomics are especially used in the healthcare related application areas, whereas food and feed related applications utilizes all but those technologies.

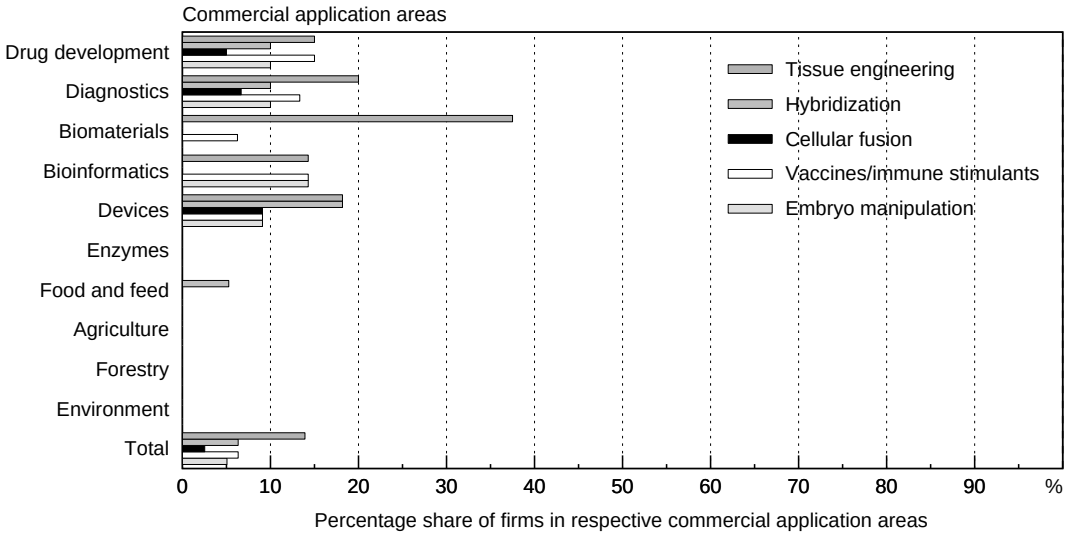


Source: ETLA Biotechnology Survey 2004.

Figure 3.3.2. The fields of commercial applications and technologies related to functional blocks of proteins and molecules.

3.3.3 Cell/Tissue culture

Tissue engineering was coined at a National Science Foundation –sponsored meeting in 1987, and later defined as "…the application of principles and methods of engineering and life sciences toward fundamental understanding …and development of biological substitutes to restore, maintain and improve [human] tissue functions (Sittinger, Hutmacher *et al.*; ETES 2005; NSC 2005; TESI 2005). Applications are found especially in biomaterials, but also in other fields of health areas as well as devices.



Source: ETLA Biotechnology Survey 2004.

Figure 3.3.3. The fields of commercial applications and technologies related to cell and tissue cultures.

Common technologies in **hybridization** are northern and southern blot (hybridization), and **embryo manipulation** can be performed in embryos originating both from animals and humans, with major ethical considerations especially around [human] stem cell research. **Cellular fusion** technology might constitute a novel means for gene therapy in the future (Daley 2004). These techniques seem to be relatively evenly used in the field of healthcare, but not in other application areas.

Finally, **vaccines/immune stimulants** are used in healthcare related applications.

3.3.4 Process biotechnologies

Process biotechnologies emerged largely with the uncovering of the molecular details of cell processes. They can be applied in a variety of settings, ranging from the manufacturing of human insulin to biodegradable plastics, and laundry detergent enzymes to hepatitis B vaccine. Typically, the technology used comes from other areas of biotechnological research and development, but the industrial scale setup is achieved though specific knowledge in bioprocessing. An example thereof is the combination of microbial fermentation with recombinant DNA technology. The distinction between process biotechnology and other techniques can be hard to establish.

The main application areas of process biotechnology are, however, usually found within agriculture, forestry, enzymes, and food and feed, that is, the field of green and white biotechnology. Energy production and energy saving applications, as well as environmental issues, are under special focus in Finland (Söderlund 2005; VTT 2005).

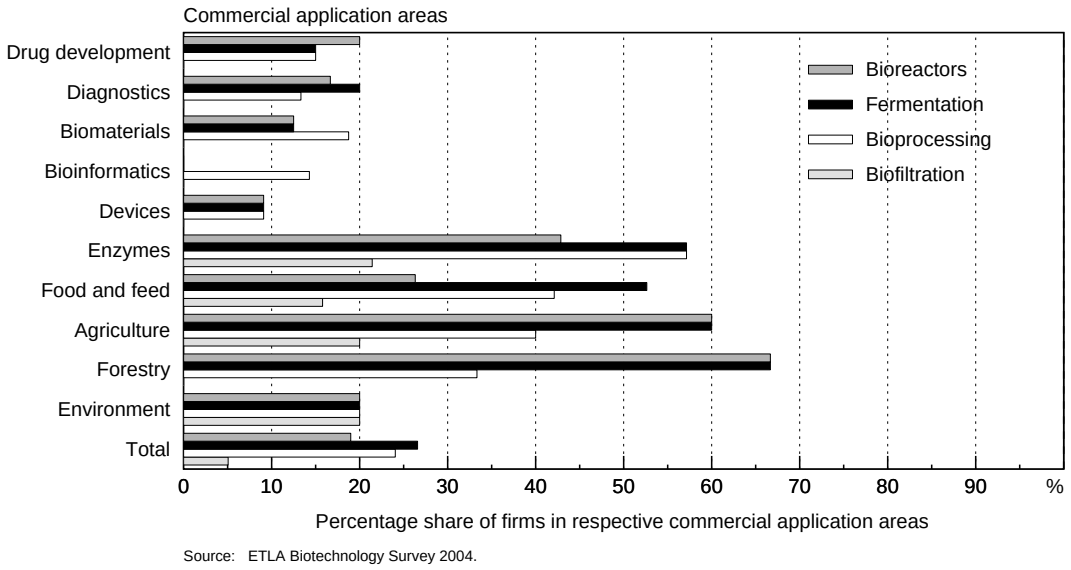


Figure 3.3.4.a The fields of commercial applications and technologies related to process biotechnologies.

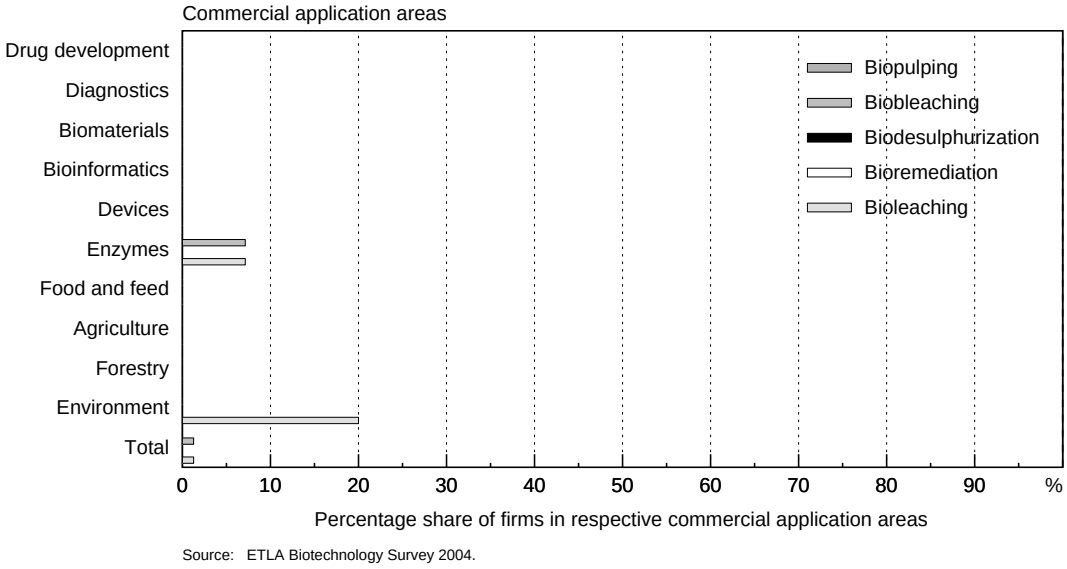


Figure 3.3.4.b The fields of commercial applications and technologies related to process biotechnologies.

Our data show that Bioreactors, fermentation, bioprocessing, and to a lesser extent biofiltration, are used in all three areas of biotechnology. The other technologies are only incidentally applied. Biopulping, biobleaching, bioleaching and also bioremediation usually have very specific application areas, and the respective companies might not belong to the classification biotechnology SMEs. Examples are the large forest and energy companies (DOE; Moreira, Feeijo *et al*.; Dyadic 2002; Holder, Stanek *et al*. 2002)

3.3.5 Sub-cellular organisms

Gene therapy encompasses at least four types of applications of genetic engineering for the insertion of genes into humans: somatic cell gene therapy, germ line gene therapy, enhancement genetic engineering, and eugenic genetic engineering. Somatic cell engineering is technically the simplest, and human clinical trials have been started for the treatment of diseases such as severe immunodeficiencies, many types of tumours (e.g. melanoma, prostate, ovarian, brain and lung cancer), AIDS, and cardiovascular disorders. Germ line cell therapy is both technically and ethically more challenging, and enhancement genetic engineering as well as eugenic genetic engineering present significant and troubling ethical concerns in addition to the technical issues.(Anderson 1985; Anderson 1992)

Viral vectors are usually associated with gene therapy, where the viral vector is used to introduce the foreign DNA to the cell. However, viral vectors can also be used in the study of *e.g.* plant cells.

Figure 3.3.5. shows a connection between gene therapy and viral vectors, which seems logical also from a technological point-of-view. The application areas are found within the field of healthcare. The connection to enzyme applications remains somewhat unclear; it could also refer to intracellular enzymes such as ribonucleases, instead of industrial enzymes as defined in the white biotechnology sector.

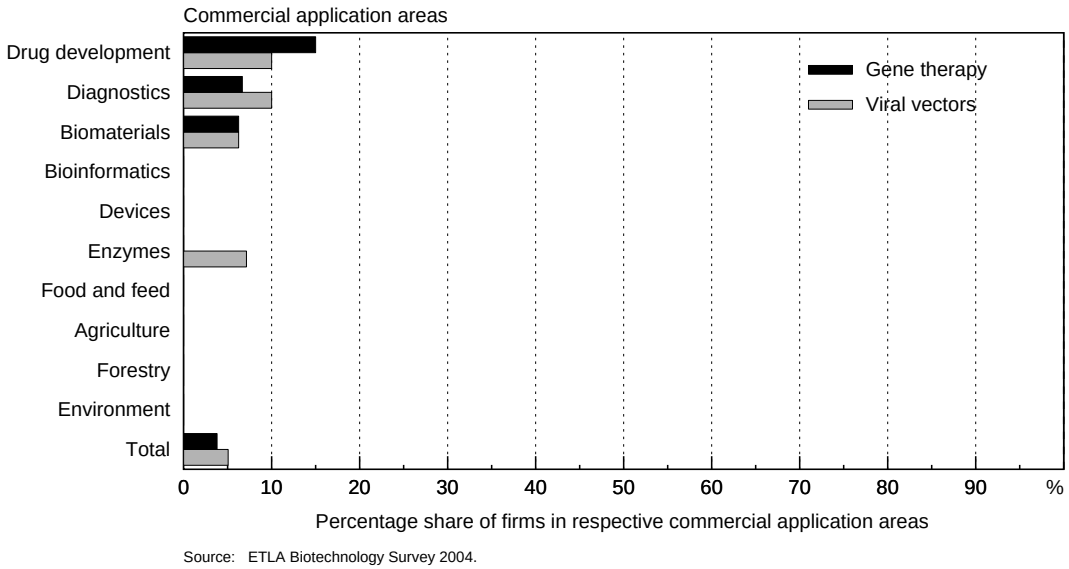


Figure 3.3.5 The fields of commercial applications and technologies related to sub-cellular organisms.

3.4 Financial Resources

Small and medium-sized Finnish biotechnology companies rely on equity for 64.5% of their financing when sales earnings are not included in the calculations. Biotechnology SMEs rely heavily on capital loans, 25.1 percent of the total funding. SMEs in general capital loans are a very marginal funding source with just 1.9 percent in 2001 within the entire economy of Finland. Capital loans are more expensive than conventional debt but do not have to be paid back if the profit situation does not allow for it. Capital loans are therefore more suitable for firms operating in high-risk investment projects such as the biotechnology sector. The relative importance of capital loans to debt is noticeable, while biotechnology SMEs rely on debt only for 10.3 percent of their funding.

3.4.1 Equity Financing

Equity financing is the main financial instrument of the small and medium-sized biotechnology companies in Finland. The Finnish companies have obtained 233 million euros in terms of equity capital from their owners (Table 3.4.1). The largest owner group is **private venture capital companies**. They own 27 percent of the companies. **Companies' personnel and external individuals** (combined to form the class **Individuals** in the following tables) form the second largest owner group with a 24 percent ownership share. **Governmental venture capital institutions** form a significant player group in the field. The most active player from this group has recently been Sitra, the Finnish National Fund for Research and Development, of which ownership share is almost 15 percent of the biotechnology SMEs. **Other companies** own over 17 percent of the industry.

Table 3.4.1.a Ownership structure by human capital (HC). [5]

HC variables	Individuals	Governmental VC	Private VC	Other companies	Other	**Total**
Personnel < 10 (n=30)	1.8 %	1.1 %	0.8 %	1.1 %	0.0 %	**4.9 % (11.4 meur)**
Personnel ≥ 10 (n=37)	22.3 %	17.7 %	26.4 %	16.3 %	12.3 %	**95.1 % (221.7 meur)**
Doctors per personnel < 22% (n=32)	18.4 %	6.7 %	21.0 %	16.3 %	4.3 %	**66.7 % (155.5 meur)**
Doctors per personnel ≥ 22% (n=35)	5.7 %	12.1 %	6.3 %	1.1 %	8.1 %	**33.3 % (77.6 meur)**
Total	**24.1 %**	**18.9 %**	**27.3 %**	**17.4 %**	**12.4 %**	**100.0 % (233.1 meur)**

Company's personnel and external individuals own the largest share of the micro-sized Finnish biotechnology companies, with fewer than 10 employees (Table 3.4.1). In medium-sized companies with 10 or more employees, **private venture capital companies** have invested the largest share in terms of equity financing. The equity financing seem to have enabled the growth of the companies, since 95 percent of the financing has been directed at companies, with 10 or more employees at the end of 2003. However, the preferences of the distinctive investor groups seem to differ in accordance with the level of education of the company's human capital. **Governmental venture capital institutions**, mainly Sitra, and the group of **other Investors** have preferred to invest in companies with a large share of exceptionally highly educated personnel. By contrast, **other companies**, **private venture capital companies** and **individuals** have directed mostly their investments to the companies with smaller doctor-to-personnel ratios.

Table 3.4.1.b Ownership structure by structural capital (SC).

SC variables	Individuals	Governmental VC	Private VC	Other companies	Other	**Total**
IPRs < 4 (n=32)	2.6 %	1.5 %	1.6 %	0.6 %	0.1 %	**6.4 % (14.9 meur)**
IPRs ≥ 4 (n=35)	21.5 %	17.3 %	25.7 %	16.8 %	12.2 %	**93.6 % (218.2 meur)**
IPRs per personnel < 0,3 (n=32)	13.2 %	3.7 %	3.0 %	12.0 %	4.9 %	**36.7 % (85.6 meur)**
IPRs per personnel ≥ 0,3 (n=35)	11.0 %	15.1 %	24.3 %	5.4 %	7.5 %	**63.3 % (147.5 meur)**
Total	**24.1 %**	**18.9 %**	**27.3 %**	**17.4 %**	**12.4 %**	**100.0 % (233.1 meur)**

[5] Our sample with full information on the sources of financing contains 67 companies. The sample is weighted to match the population (see also Hermans and Tahvanainen 2002). We used the following definition for equity: Equity equals the stockholders' paid-in equity capital and equity reserves obtained from National Board of Patents and Registration of Finland. We ignored the cumulative profits of past financial years. This is due to the idea that even when firms' balance sheets are distorted by great losses, they do not necessarily reflect the level of expected earnings. Negative equity figures distort also the counting of equity shares. If we take official paid-in capital figures on stockholders' equity we get the value that stockholders' have invested in a company. Accordingly, we do not consider earnings as part of equity financing in this study.

We measured Intellectual Property Rights (IPRs) as the number of patent applications and patents. **Investors** have invested almost 94 percent of total equity in the companies with 4 or more patents and applications in their patent portfolios. **Individuals** own the largest share of the companies with small patent portfolios. When we use patents and the patent applications-to-personnel ratio, the scheme changes. **Individuals** and **other companies** hold the largest share of those biotechnology companies that do have a relatively small IPR to personnel ratio; and **governmental venture capital institutions** and **private venture capital companies** have directed their investments to the companies with higher IPR intensity.

Table 3.4.1.c Ownership structure by relational capital (RC).

RC variable	Individuals	Governmental VC	Private VC	Other companies	Other	Total
Sales < 170000 (n=30)	5.0 %	3.9 %	3.6 %	1.1 %	1.5 %	**15.3 % (35.6 meur)**
Sales ≥ 170000 (n=37)	19.2 %	14.9 %	23.7 %	16.3 %	10.9 %	**84.7 % (197.6 meur)**
No R&D collaboration with foreign university (n=46)	6.6 %	7.4 %	9.1 %	4.3 %	1.8 %	**29.2 % (68.0 meur)**
R&D collaboration with foreign university (n=21)	17.5 %	11.4 %	18.2 %	13.1 %	10.6 %	**70.8 % (165.1 meur)**
Total	**11.8 %**	**14.7 %**	**27.3 %**	**17.4 %**	**12.4 %**	**100.0 % (233.1 meur)**

Other companies have focused their equity financing most clearly towards the firms whose sales have reached relatively high volumes; or, they have been able to strengthen the exporting skills of the companies they own. International trade volumes seem to go quite closely hand in hand with international R&D collaboration. There are only 21 companies, 31 percent of the companies in our sample, which collaborate with foreign universities, but these have obtained over 70 percent of the total equity financing.

3.4.2 Capital Loan Financing

Capital loans are loans that satisfy the regulations enacted in the Finnish Companies Act. The act states that capital loans must be included in the shareholders' equity in the financial statement. In other words, capital loans are a mixture of financial instruments of debt and equity. Capital loans can be used to prevent a company from being adjudicated to bankruptcy, because they are defined as equity capital in the balance sheet despite their nature of debt. Thus, the increase of capital loans compensates past losses as a supplement to equity capital.

Table 3.4.2.a Capital loan structure by human capital (HC).

Capital loan structure by human capital (HC)	Domestic banks	Governmental VC	Domestic private VC	Foreign VC	Other Firms	Finnvera	Tekes	Others	**Total**
Staff (n < 10)	0.0 %	4.8 %	0.7 %	0.7 %	0.9 %	0.2 %	2.6 %	0.0 %	**10.0 % (9.1 meur)**
Staff (n ≥ 10)	2.1 %	10.0 %	0.7 %	0.2 %	2.8 %	4.7 %	61.0 %	8.4 %	**90.0 % (81.7 meur)**
Doctors per personnel < 22%	1.6 %	10.7 %	0.7 %	0.2 %	2.3 %	3.5 %	8.1 %	0.1 %	**27.2 % (24.7 meur)**
Doctors per personnel ≥ 22%	0.6 %	4.1 %	0.7 %	0.7 %	1.4 %	1.5 %	55.5 %	8.4 %	**72.8 % (66.1 meur)**
Total	**2.2 %**	**14.8 %**	**1.5 %**	**0.9 %**	**3.7 %**	**4.9 %**	**63.5 %**	**8.4 %**	**100,0 % (90.8 meur)**

The small biotechnology industry has obtained over 90 million euros in capital loans constituting 25.1 percent of total funding. Thereby it is an important backbone, vital for the survival of companies. The largest single capital loan provider is Tekes, the National Technology Agency of Finland. Tekes has provided nearly 60 million euros in terms of capital loans to the biotechnology companies. Tekes invests typically in research-intensive projects, whereas, other companies invest in the projects which are already closer to markets. Thus, the projects closer to markets employ human capital related to other competencies than solely to academic research.

Table 3.4.2.b Capital loan structure by structural capital (SC).

Capital loan structure by structural capital (SC)	Domestic banks	Governmental VC	Domestic private VC	Foreign VC	Other Firms	Finnvera	Tekes	Others	**Total**
IPR < 4 pcs	0.0 %	4.3 %	1.5 %	0.2 %	0.5 %	0.5 %	4.4 %	0.1 %	**11.5 % (10.5 meur)**
IPR ≥ 4 pcs	2.2 %	10.5 %	0.0 %	0.7 %	3.2 %	4.4 %	59.1 %	8.4 %	**88.5 % (80.3 meur)**
IPR/Staff < 0.3	1.5 %	6.2 %	0.7 %	0.2 %	2.8 %	0.3 %	17.4 %	7.5 %	**36.7 % (33.3 meur)**
IPR/Staff ≥ 0.3	0.6 %	8.6 %	0.7 %	0.7 %	0.9 %	4.6 %	46.1 %	1.0 %	**63.3 % (57.4 meur)**
Total	**2.2 %**	**14.8 %**	**1.5 %**	**0.9 %**	**3.7 %**	**4.9 %**	**63.5 %**	**8.4 %**	**100,0 % (90.8 meur)**

Except for Finnvera that seems to follow a similar capital loan strategy as Tekes, no such obvious investment policies can be observed by other capital loan providers. It seems clear that higher amount of IPRs are strictly related to capital loans invested in the companies. This is rather intuitive since IPRs are traditionally considered a simple (and often sole) indicator of innovativeness and commercialization potential in practice.

Table 3.4.2.c Capital loan structure by relational capital (RC).

Capital loan structure by relational capital (RC)	Domestic banks	Governmental VC	Domestic private VC	Foreign VC	Other Firms	Finnvera	Tekes	Others	**Total**
Sales < 170,000	0.6 %	12.3 %	0.7 %	0.7 %	0.9 %	1.4 %	44.2 %	8.4 %	**69.3 % (62.9 meur)**
Sales ≥ 170,000	1.5 %	2.5 %	0.7 %	0.2 %	2.8 %	3.6 %	19.3 %	0.1 %	**30.7 % (27.9 meur)**
No collaboration with foreign university	1.6 %	8.9 %	1.5 %	0.2 %	1.4 %	0.9 %	13.2 %	7.5 %	**35.2 % (32.0 meur)**
Collaboration with foreign university	0.6 %	5.9 %	0.0 %	0.7 %	2.3 %	4.0 %	50.4 %	1.0 %	**64.8 % (58.8 meur)**
Total	**2.2 %**	**14.3 %**	**1.5 %**	**0.9 %**	**3.7 %**	**4.9 %**	**63.5 %**	**8.4 %**	**100,0 % (90.8 meur)**

Tekes's acknowledging stance towards the concept of a well-balanced intellectual capital base as a key success factor for knowledge-intensive organizations restates itself in the distributions of capital loan sources by the two remaining IC components. Tekes clearly prefers companies that display higher levels of structural and relational capital. However, in biotechnology the balanced intellectual capital palette has not been able to create high volumes of sales in the companies. This probably reflects the problem of the recent revenue creation in the Finnish biotechnology as a whole.

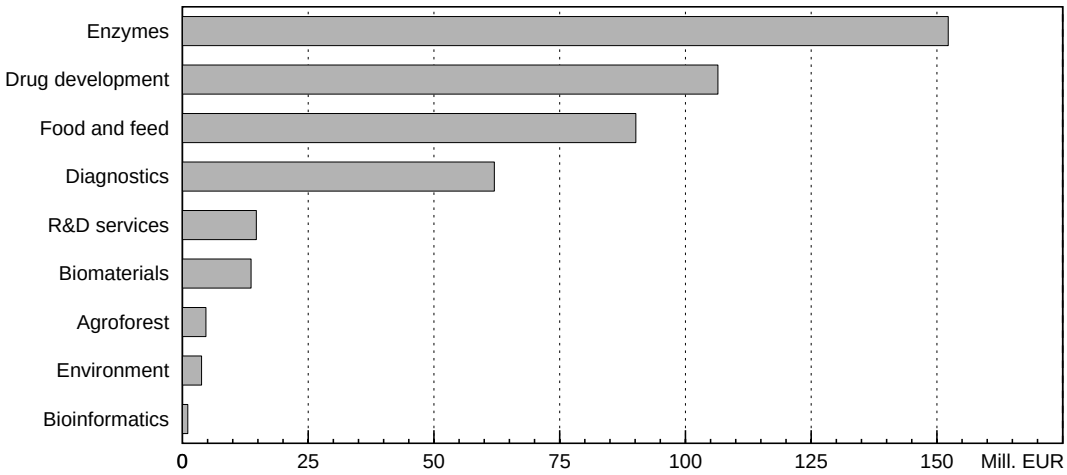
3.5 Value Creation of Intellectual Capital

Total sales of the small biotechnology industry reached 330 million euros in 2003 (Table 3.5) leaving the industry still unprofitable. Operating losses were 60 million euros during this period and net losses 70 million euros.

Table 3.5 Sales and profitability of the small Finnish biotechnology industry in 2003.

	Million euros
Sales	332
Operating profits	-60
Net profits	-70

Revenues were highest in enzymes -one of the most traditional sectors of Finnish biotechnology- followed by drug development and food and feeds. With over 150 million euros, enzymes make up almost half of all revenues of the small biotechnology industry. Bioinformatics is last with compound revenues of less than 3 million euros.



Source: ETLA Biotechnology Survey 2004.

Figure 3.5 Sales of the Finnish biotechnology industry by the fields of applications in 2003.

3.6 Regional context

3.6.1 Competence Base and R&D Collaboration

Collaboration in research and development is crucial in many aspects for the success of research-intensive companies. As the human capital of a particular company is limited to that provided by people employed and committed to the company, a possible lack of abilities, experience, and skills needed for a successful completion of R&D projects must be compensated for by accessing external sources.

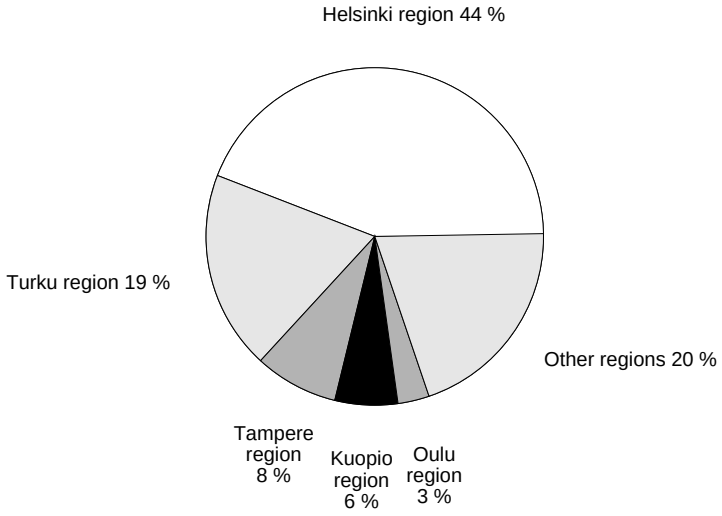
While the human capital requirements differ from project to project, its supply has to be flexible for the company in order to be able to retain as lean a cost structure as possible -an ultimate requirement for young research-intensive companies often without internally generated revenue streams.

As opposed to hiring ever new employees to compensate for lacking human capital, collaboration with other organizations provides several advantages. Firstly, compensation between collaboration partners does not necessarily require monetary flows during the project. Partners, for instance, agree on splitting future revenues generated by the outcome of the project according to the amounts of input provided by each partner. Secondly, instead of acquiring the limited abilities of single individuals, collaboration provides access to the collective of generative intangibles of the partner with a far higher potential of creating value by definition than can be provided by additional individuals employed. Finally, partners can be chosen with project specific requirements in mind and, even more importantly, released from the collaboration after the completion of the project or an *ex ante* specified part of it, resulting thereby in the flexibility spoken of above.

Mowery (1998) summarizes additional advantages of collaboration as suggested by the economics literature in general. These include the ability to capture knowledge-

spillovers by collaboration partners that might be otherwise wasted, the reduction of R&D duplication and thereby saving of resources invested into it, the utilization of scale economies in R&D, the acceleration of commercialization of new technologies, a quicker transfer of technology from universities and other research organization to the industry, an enhanced access to capabilities of these organizations by the industry, and lastly, the chance to establish a common technological vision among the industry that results in a more focused and structured approach towards it.

Literature suggests that there is a clear negligence concerning the potential advantages of collaboration in biotechnology (see Shan, Walter and Kogut 1994, Nilsson 2001 as well as Powell 1998). A too introvert attitude compromises the ability of firms to identify and capture emerging opportunities, be they technological or commercial, in the absence of a supportive and complementary network. With these thoughts as a backdrop the collaboration patterns of sample companies present themselves in Figures 3.6.1.a-f.



Source: ETLA Biotechnology Survey 2004.

Figure 3.6.1.a Share of labor employed by the small biotechnology industry in the Finnish regions in 2003.

In order to be able to speak about geographical R&D collaboration patterns, a sense of local volumes in R&D -proxied by the number of employees- has to be established first. Figure 3.6.1.a. gives a comprehensive distribution of the shares of total employment in the SME biotechnology industry by domestic regions. The Helsinki region is by far the biggest employer with nearly 45% of total employment, followed by Turku with less than half the size, Tampere, Kuopio and Oulu. As already stated, the small biotechnology industry employs about 2500 individuals in total.

Figure 3.6.1.b. presents a geographical display of the number of firms collaborating between any two domestic regions. On a global scale, domestic collaboration is the single most important region for Finnish biotechnology firms, with 94,5% of companies collaborating with a partner inside Finnish borders. In the figure, the thickness of the connecting lines is proportional to the number of collaborating firms. As one might expect from looking at the distribution of employment, the number of firms collaborating with each other is highest between the capital area and Turku region. Further, the Helsinki

region seems to constitute a particularly important collaboration knot as there is a high amount of collaboration between this region and every other major region, as well as many of the most peripheral regions. No other region exhibits as many collaborating companies. The question whether this is an effect caused by the sheer volume of biotechnology in the Helsinki region or whether firms in the region are actually more actively seeking collaborative arrangements is an issue for future analysis.

Of the five major biotechnology regions in Finland, Tampere seems to be the most inactive collaborator as expressed by the number of collaborating companies. Collaboration among companies in the peripheries is rather rare, although not completely non-existent.

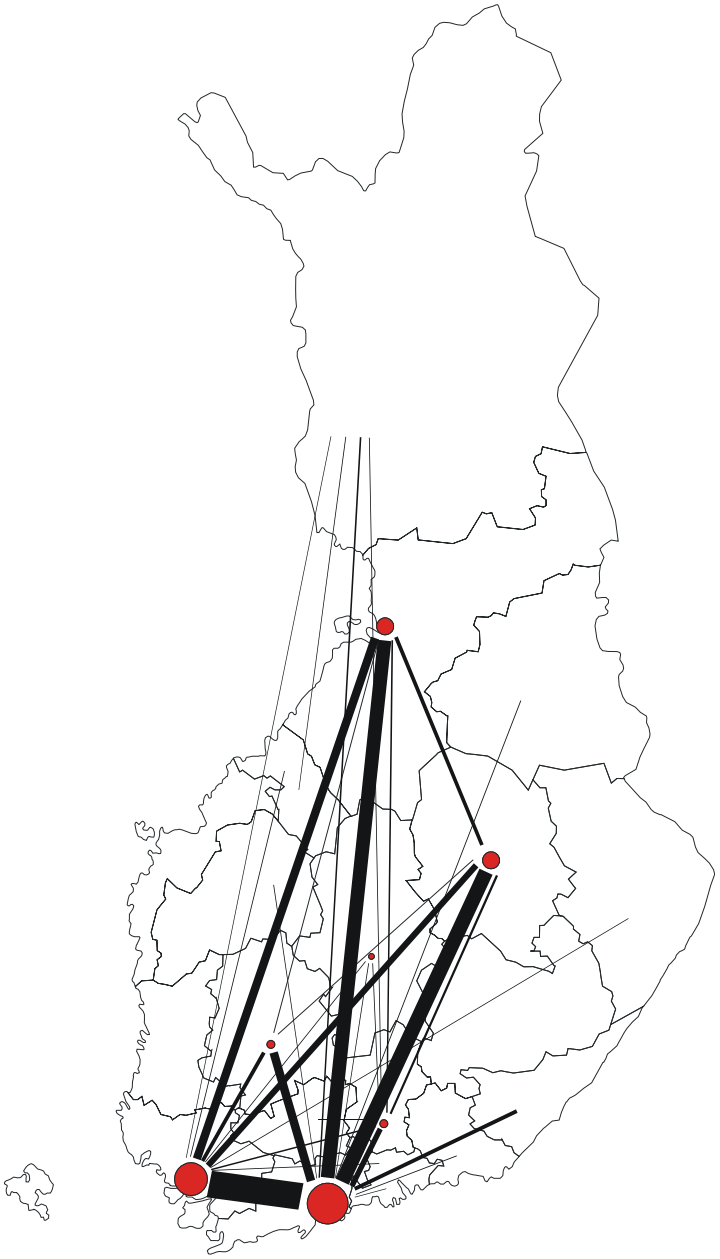


Figure 3.6.1.b Domestic R&D collaboration of the Finnish biotechnology industry in 2003

Figure 3.6.1.c is a graphical illustration of R&D collaboration volumes to regions outside Finland. These regions are the EU, North America, and Asia. For reasons of geographical clarity we have included firms from the five major domestic biotechnology centers only, as peripheries have little effect on the results. Again, the thickness of the arrows indicates the number of firms collaborating with the particular foreign region. It is obvious that the EU region (downward arrow) represents the major foreign region of collaboration for Finnish biotechnology companies with 57,5% of sample companies having collaborating arrangements with EU companies outside Finland.

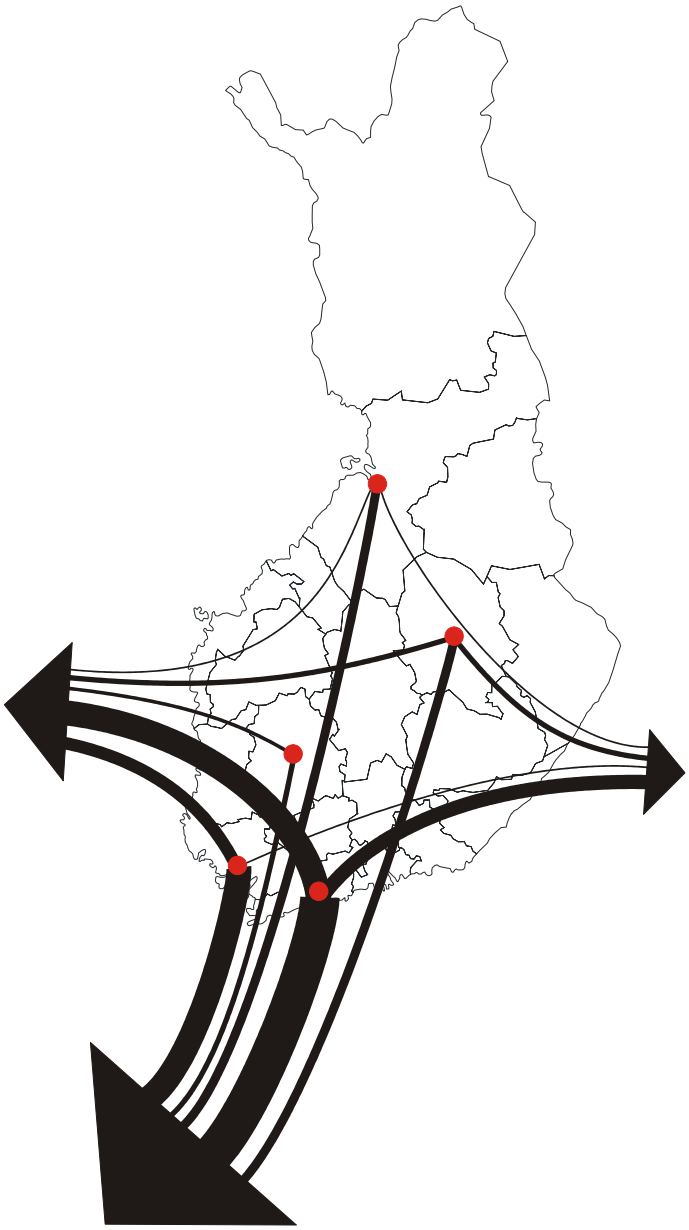


Figure 3.6.1.c International R&D collaboration of the Finnish biotechnology industry in 2003.

North America represents the second most important region with 30% of the sample companies having R&D partners in the region. In particular, firms active in equipment development (45% of sample companies in this sector), drug development (33%) and contract production (31%) have established partnerships in North America. Enzymes, food and feeds, as well as diagnostic services, follow closely with just below 30% of them having collaboration partners in this region.

Asia constitutes a less frequent region of collaboration in R&D, with 14% of all sample companies displaying collaboration arrangements with the Asia-Pacific region. Enzymes and food and feeds are the sectors in which R&D collaboration is most frequent with this region.

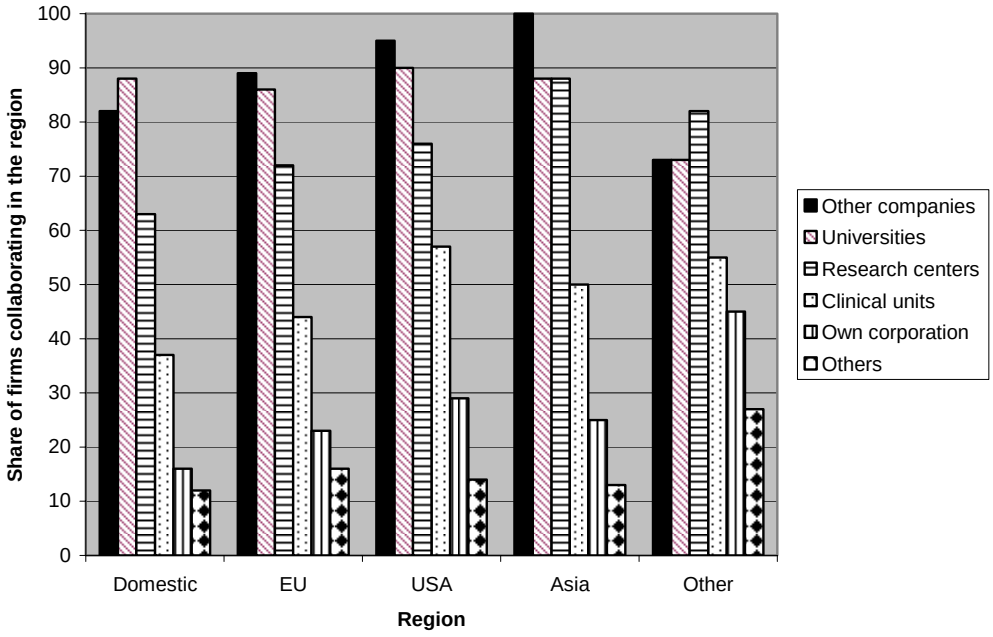


Figure 3.6.1.d Collaboration partners by region

Figure 3.6.1.d shows the type of collaboration partners as encountered in the different collaboration regions worldwide. It is striking that the relative frequency of partner types remains almost constant from region to region. It seems that no region can boast a comparative advantage in offering better opportunities or a higher quality of supply in any type of collaboration partnership. Other companies (clients, sub-contractors, competitors, venture partners, and so forth) seem to be the most frequent type of partner in every region except on domestic grounds.

Figures 3.6.1.e and 3.6.1.f show that age does not have an overwhelming effect on the propensity to co-operate in R&D be it by region or type of partner, except for the companies of old age (≥ 24 years) that co-operate more frequently than their younger counterparts. It seems also that the youngest companies (less than 5 years of age) have a tendency to co-operate slightly less than their older companions. The effect is amplified with the growing distance to the collaboration region.

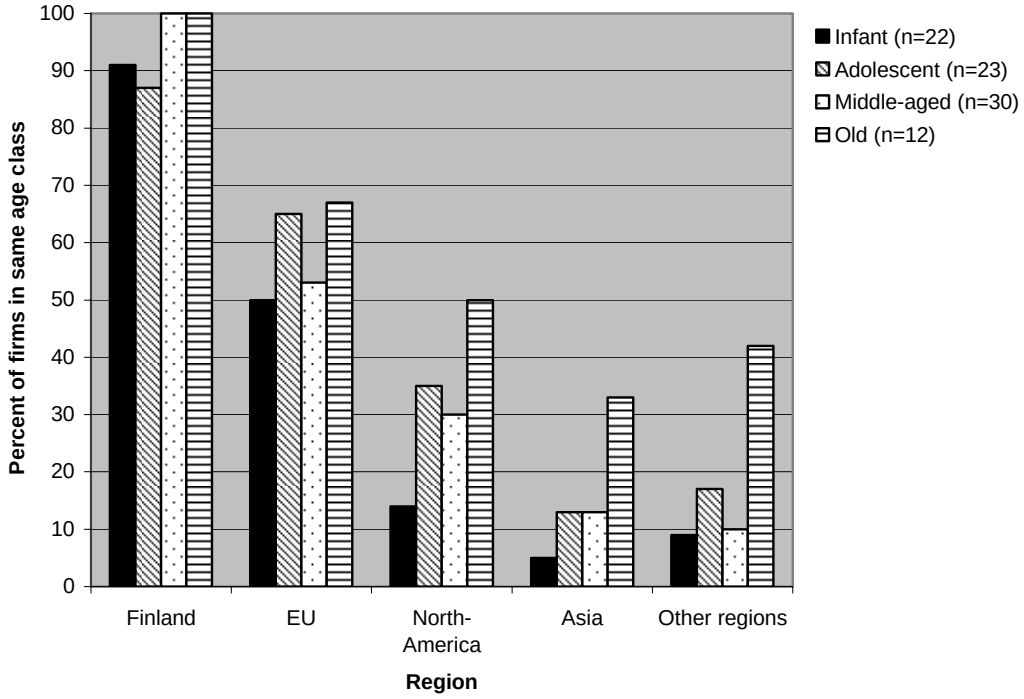


Figure 3.6.1.e R&D collaboration regions by age (Change to North America)

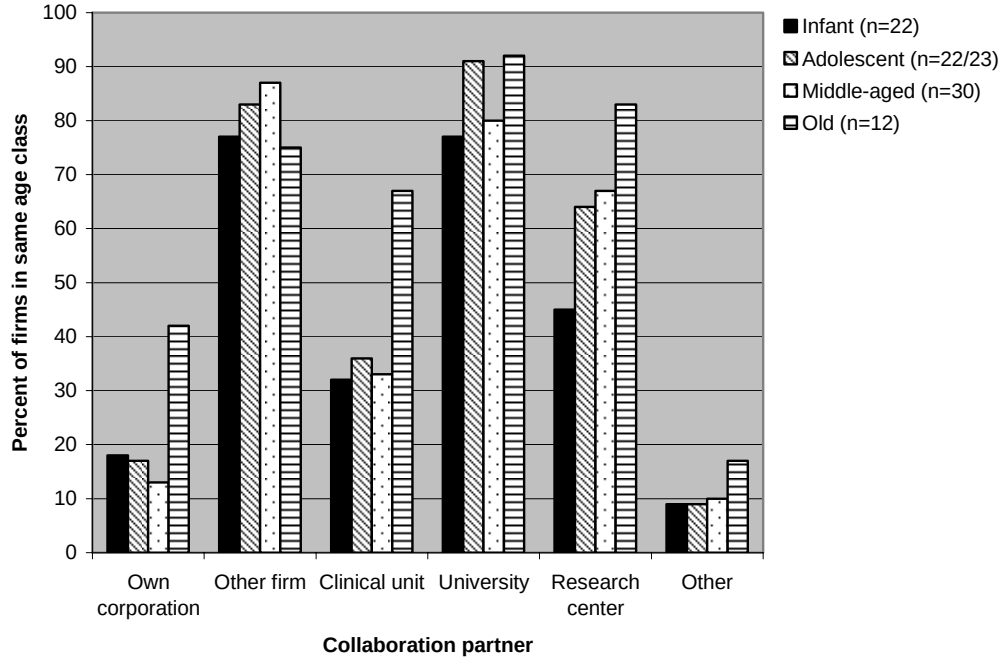


Figure 3.6.1.f R&D collaboration partners by age

3.6.2 From Innovation to Sales by Regions

Table 3.6.2 displays the shares of domestic regions of total public R&D expenditures, industry R&D expenditures and industry sales. It gives rise to two possible interpretations of their relations to each other. According to the first interpretation the Figure displays a continuum, at the beginning of which there is an amount of public money spent on basic research that then, in a second phase, induces industry led R&D, resulting in commercialization in a last phase. Following this path of interpretation, the Helsinki region has done quite well in transforming publicly financed research first into growing private product development and then succeeding in commercializing the development by conquering close to 80 percent of markets reached by Finnish biotechnology companies altogether. The relation between public money induced, private R&D generated by that, and the sales emerging from the R&D is always positive from phase to phase and seems healthy. The Helsinki region seems to create value. Turku is actively transforming publicly financed research into R&D but seems to fail in commercializing the R&D. The Kuopio and Tampere regions are on the same path as Turku although being much smaller in volume. The Oulu region seems to perform poorly as public money does not lead to industry R&D, which is to an even lesser degree commercialized.

Another way of interpreting the Figure is to look at it as a cross-section in time. Then one might say, for example, that the Helsinki region is already in a more mature state having had time to go through all three phases and having set up necessary down-stream assets and tapped into the markets. Following this interpretation Oulu might still be in an infant state of development just building up the necessary infrastructure and company base necessary for successful R&D, not to speak of commercialization. Given time, the region might then very well create value in the future. Thus, the Figure might simply be showing regions in different states of development and growing towards the markets, as Helsinki has already done.

Table 3.6.2 Relation of public R&D expenditures for biotechnology, R&D expenditures of the biotechnology industry and sales of the biotechnology industry (SMEs) by domestic regions in 2003. Source: Statistics Finland, ETLA.

	Public R&D expenditures	Industry's R&D expenditures	Industry's sales
Helsinki region	39.2 %	45.5 %	65.6 %
Turku region	18.0 %	30.9 %	7.0 %
Tampere region	10.8 %	7.0 %	2.8 %
Kuopio region	7.8 %	5.9 %	1.3 %
Oulu region	21.1 %	8.0 %	0.9 %
Other regions	3.0 %	2.6 %	22.4 %
Finland	100.0 %	100.0 %	100.0 %

4. Conclusions

This paper presents descriptive statistics based on the survey conducted at the end of 2004 by ETLA. This paper also concludes the results of the analyses derived from the Etla 2002 survey. The number of active biotechnology companies has remained stable during the last two years. In the 2004 survey we achieved an equally high response rate (over 70 percent) as in the ETLA 2002 survey. Thus, our data gives a representative overview of Finnish biotechnology SMEs.

The data has been improved. The present survey provides exact data, not estimates, on financial statements and number of employees concerning the entire population. Other new insights include geographical and inter-institutional R&D-collaboration patterns, which show that the domestic collaboration has agglomerated particularly to Southern Finland. The international collaborations show a pattern of gravitation with the same Southern regions. However, this picture may change in our further analyses taking into account a regional population distribution.

Information asymmetry is regarded as an inherent feature in biotechnology. This is at least in part a result of the several novel and complex technologies whose definitions overlap each other. Signs of this were visible also in our data. As an example, several companies were unable to position themselves correctly in the specific application fields, and many companies apparently did not know the definitions of technologies used in biotechnology research and development.

The ETLA 2004 survey contains also product-level data that incorporates R&D- and sales figures, forecasts thereof, collaboration patterns, product-specific science-base mapping, and academic origin of the innovations. Through these new features, the data enables a more thorough and detailed analysis of the sector than could have been carried out before. In further studies, we will present the anticipated future sales and risk profiles of the companies based on the product-level data.

Further research is also needed to evaluate which potential niches the biotechnology sector should seek to fill when developing products with commercial potential. When seeking to identify these niches, it is important to keep in mind that the competence base must be sufficiently large to generate the critical mass necessary for spawning products and services with sufficiently large market potential. We can look at the preconditions for turning research into commercial products from the standpoint of the competence base underlying this critical mass: knowledge-intensive entrepreneurship, financing possibilities, and international market potential

1) by distinguishing the main incentives and barriers regarding entrepreneurship in a research segment with a deep competence base. In addition, by investigating the distribution of biotechnology companies that have already emerged, we might find niches that have a considerable competence base as well as a “commercialization gap”.
2) by analyzing the preferences of financiers investing in biotechnology companies, which is then compared with the distribution of the competence base of biotechnology research.

3) by analyzing and comparing the international market potential to Finland's competence base.

Such further research would be beneficial for planners of general technology policies and actors in various sub-sectors of the biotechnology industry. Technology policy experts can benefit from the research results when gauging use of alternative types of aid in light of the principle of comparative advantage based on international trade analysis. In Finland, substantial amounts of state aid are directed to the biotechnology sector; however, the private and public investment activity is rather modest by international standards. Resources should thus be allocated prudently.

Biotechnology research can be applied in many diverse areas. There is a danger that when making financing decisions the authorities are unable to "see the forest for the trees". Therefore, start-ups that base their activities on isolated top-notch research fields may end up without financing. A reason can be the lack of a viable business plan even if the segment has considerable market potential.

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The term 'gene therapy' encompasses at least four types of application of genetic engineering for the insertion of genes into humans. The scientific requirements and the ethical issues associated with each type are discussed. Somatic cell gene therapy is technically the simplest and ethically the least controversial. The first clinical trials will probably be undertaken within the next year. Germ line gene therapy will require major advances in our present knowledge and it raises ethical issues that are now being debated. In order to provide guidelines for determining when germ line gene therapy would be ethical, the author presents three criteria which should be satisfied prior to the time that a clinical protocol is attempted in humans. Enhancement genetic engineering presents significant, and troubling, ethical concerns. Except where this type of therapy can be justified on the grounds of preventive medicine, enhancement engineering should not be performed. The fourth type, eugenic genetic engineering, is impossible at present and will probably remain so for the foreseeable future, despite the widespread media attention it has received.

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Human gene therapy is a procedure that is being used in an attempt to treat genetic and other diseases. Eleven clinical protocols are under way at the present time, each with scientific and clinical objectives. Human genetic engineering raises unique safety, social, and ethical concerns.

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Appendix: Examples of healthcare biotechnologies as presented by EuropaBio

Cell and tissues

A person's own cell and tissue can offer a patient a wide range of healthcare solutions, from prosthetic and restorative to therapeutic or even cosmetic in nature. Under normal conditions damaged joint cartilage does not – or only poorly - regenerates in the body. For several years now, cell therapy for restoring defects to knee cartilage has been available by growing a patient's own cartilage cells to repair cartilage defects. Active research, involving human cell-and tissue-based products, is currently being conducted in the regeneration and repair of bones, tendons, nerves, and ligaments.

Cell-based cancer immunotherapy like cell-based tumor vaccines to combat cancer are providing compelling news that such therapy may one day provide hope for cancer patients.

Stem cells

Research into stem cells may result in important cell-based therapies to treat serious diseases and conditions like Parkinson's disease, Alzheimer's disease, spinal cord injuries, as well as diabetes, stroke, burns, skin disorders, and heart disease. Researchers work on three types of human stem cells – adult, fetal, or embryonic. The use of human embryonic stem cells raises important questions, which are currently at the center of an ethical and societal debate.

Gene therapy

Despite the high standard of today's medical treatments, and the number of already available drugs, many of the most debilitating human diseases do not have a cure yet. The molecular basis of many inborn disorders, such as hemophilia, cystic fibrosis, or muscular dystrophy, has been exposed by the discovery of affected genes. In many forms of cancer, genetic predisposition plays as important a role as environmental factors in tumor growth, and malignancy. Identifying the gene for such diseases and redirecting its course is one of the most promising ways to cure certain diseases.

Gene therapy has entered a phase of active clinical investigation in many areas of medicine. Human clinical trials have been started for the treatment of severe immunodeficiencies, cystic fibrosis, hypercholesterolemia, hemophilia, muscular dystrophy, many types of tumors (e.g. melanoma, prostate, ovarian and lung cancer), AIDS, and cardiovascular disorders.

Unmet medical needs

"Healthcare biotech responds to patients' unmet medical needs"

Today there are many more diseases than treatments. Just 10 000 of the 30 000 known diseases have treatments available. Greater understanding of disease and the causes of disease is helping to produce better therapies that can more effectively address medical needs. New insights into the biology of disease, and a more precise understanding of why some people react differently, lie at the heart of biotechnology. The promise of more targeted treatments to individual groups of patients, as well as providing treatments for diseases that so far have eluded treatment, are providing us with new opportunities to meet challenging but common diseases like heart disease, cancer, and Alzheimer's, as well rare diseases.

Rare diseases and orphan drugs

Some 20-30 million Europeans are affected by 5000 rare diseases. Biotechnology provides powerful tools to develop diagnostics and treatments for orphan diseases.

Since the EU Orphan Drugs Regulation came into force in early 2000 it has covered over 212 applications for orphan drugs designation. The Committee for Orphan Medicinal Products (COMP) at the European Medicines Evaluation Agency (EMEA) has adopted opinions on 167 of these and the Committee for Proprietary Medicinal Products (CPMP) at the EMEA has provided positive opinions for the marketing approval of 13 designated orphan drugs, of which 9 were already approved by the European Commission by August 2003. They are:

- Fabrazyme & Replagal (both for the treatment of Fabry disease, a lysosomal storage disorder)
- Gleevec (for the treatment of chronic myeloid leukaemia)
- Tracleer (authorization pending – for the treatment of pulmonary arterial hypertension)
- Trisenox (for the treatment of acute promyelocytic leukaemia)
- Zavesca (for the treatment of Gaucher Disease)
- Somavert (for the treatment of acromegaly)
- Aldurazyme (for the treatment of Mucopolysaccharidosis type 1)
- Busilvex (for the conditioning treatment prior to hematopoietic progenitor cell transplantation).
- Carbaglu (for the treatment of N-acetylglutamate synthase deficiency)

Proteomics

Proteomics is the science which studies the physiological function of proteins and their effects on diseases. Some diseases are caused if genes do not produce the proteins (or enough proteins) the body requires or if the body produces wrongly folded proteins. Biotechnology is using recombinant (artificially created) DNA (See definitions) and cell cultures to produce missing or defective proteins. Replacement protein therapies include Factor VIII-a protein essential for the blood-clotting process and which some hemophiliacs lack, or insulin - a protein hormone that regulates blood glucose levels.

A great deal of research is ongoing to determine the role that proteins play both in the cause and cure of disease.

Tailor-made medicines

"Healthcare biotech can tailor medical treatment to patients"

For patients, finding the right medication with less trial and error is critical. Healthcare biotechnology is helping to bring made to measure treatments to patients.

Pharmacogenetics

Pharmacogenetics studies the effect genes may have on an individual's response to a drug. Pharmacogenetics uses biotechnology-based technologies to not only better diagnose disease, but also to provide new ways to match medicine doses and medical treatments to individual groups of patients. The evolving area of pharmacogenetics will increase both the safety and efficacy of treatments by diminishing the trial and error for patients trying to find the optimal dose and treatment. Pharmacogenetics holds great promise to offer more select drugs to treat elusive variations of common as well as rare diseases and widen the numbers of diseases that can be treated effectively, as well as limiting the occurrences of adverse drug reactions on patients.

Improvements in diagnosis

"Healthcare biotech can help prevent and better diagnose disease"

Patients often have difficulty in getting a correct diagnosis. Biotechnology is offering new tools to doctors and patients to provide better diagnosis and more effective but less intrusive and uncomfortable testing for patients.

Diagnostics

We can now detect many diseases and medical conditions more quickly and with greater accuracy due to the sensitivity of new, biotechnology-based diagnostic tools. A familiar example of biotechnology's benefits is the new generation of home pregnancy tests that provide more accurate results much earlier than previous test-generations.

Another good example is PCR technology: The Polymerase Chain Reaction (PCR) is a technology that imitates a cell's ability to replicate DNA by generating multiple copies of specific sequences of DNA through amplification. In clinical diagnostics, a specimen of genetic material weighing only one-trillionth of a gram can be repeatedly copied by PCR to provide sufficient material to detect the presence or absence of a virus as well as to quantify its levels in the blood. PCR tests were the first that could accurately measure the amount of HIV in a patient's blood. This provides reliable information on the disease course and shows when changes are needed in a patient's medication.

A new blood test has been developed through biotechnology to measure the amount of low-density lipoprotein (LDL), or "bad" cholesterol, in blood. The new biotech test measures LDL in one test, and fasting is not necessary. We now use biotechnology-based tests to diagnose certain cancers, such as prostate and ovarian cancer, by taking a blood sample, eliminating the need for invasive and costly surgery.

The human health benefits of biotechnology detection methodologies go beyond disease diagnosis. For example, biotechnology detection tests screen donated blood and organs for the pathogens that cause AIDS, hepatitis, and a variety of other infectious diseases.

Doctors will someday be able to immediately profile the infection being treated and, based on the results, choose the most effective antibiotics.

Genetic testing

The wealth of genomics information made available by the Human Genome Project is greatly assisting doctors in diagnosing hereditary diseases. There are currently over a thousand human hereditary diseases that can be identified using genetic tests. The majority of these tests detect the presence of a mutation or mutations in a single gene which lead to monogenic (single gene) disorders, most of which are relatively rare diseases.

Unlike monogenic diseases, there are many diseases caused by a combination of environmental factors and one or more hereditary factors. Many common diseases that affect many millions of people arise through complex interactions between the environment and a number of alternative genes called susceptibility genes. Soon doctors will have access to tests for detecting susceptibility before the onset of clinical signs if patients so wish. The presence of disease susceptibility does not always cause the disease but is a risk factor for that disease, just as smoking is a risk factor for lung or heart disease. These tests will identify patients with a propensity to diseases caused primarily by environmental factors, such as diet, giving patients an opportunity to prevent the disease by avoiding the environmental triggers. Genetic testing is also critical to the development of pharmacogenetics, which uses biotechnology-based diagnostics to better diagnose disease and provide new ways to match medicine doses and treatments to the individual.

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