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Technological foresight—the use of biotechnology in the development of new drugs against breast cancer

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Abstract

The aim of the study is to demonstrate knowledge and information management as a mechanism for developing technological foresight regarding the use of biotechnology in drugs for breast cancer. The methodology applies competitive intelligence (CI) tools to identify international trends concerning drugs for treatment and/or diagnosis, and to identify leading institutions. The study was performed by collecting, treating and analyzing information extracted from specialized databases and patent databases. Subsequently, knowledge maps were generated, which could serve to guide the development of the health sector that works in the area of breast cancer, supplying a basis for decision-making and for the construction of a vision of the future. The article shows the results of data mining in specialized medical and patent databases with regard to the use of biotechnology in the treatment of breast cancer, identifying the most frequently cited new drugs and drug combinations, as well as the authors of research (articles) and the creators of new technology (patents) at the beginning of the 21st century.

Keywords: Knowledge and information management; Health sector; Technological foresight; Competitive intelligence; Breast cancer

1. Introduction

In recent years, increasing international competition has raised issues relevant to the understanding of the process of innovation, and it should be noted that the understanding that innovation consists of a process of searching and learning dependent on interactions and specific situations is a complex approach to the topic, one which has been breaking paradigms at this moment in the construction of the knowledge economy.

The economic success of any country, region or place increasingly depends on its capacity to specialize in activities which allow it to establish effective and dynamic competitive advantages, based on local competencies and capacities to learn, in the sense of creating an environment of transformation and progress, as well as the capacity to cooperate, which has become a key in innovation.

In this way, technology foresight, using the tools of knowledge and information management, based on primary and secondary sources, is extremely useful in arriving at an understanding of the state of the art of a given sector, with the goal of generating value-added information about technological and market trends and thus feeding the cycle of the creation of new wisdom. Technology foresight, based on knowledge management, is becoming increasingly valued and its systematic use is more and more being understood as an investment. Innovation in the methods and processes of management is, therefore, a challenge in the face of the changes of a globalized market, with its increased competition, high degree of uncertainty and abundance of information.

Within this new competitive paradigm, the salient features are the demands for excellence in products and services, and increases in differentiation, flexibility, speed, cost rationalization and innovation. Meeting these demands calls for new management models, and it is here that the importance of approaches such as competitive intelligence (CI), knowledge management and foresight becomes evident (Cowan et al., 2003).

Technological foresight, based on three aspects: information—technology—specialists, opens a range of opportunities which make desired futures attainable, as

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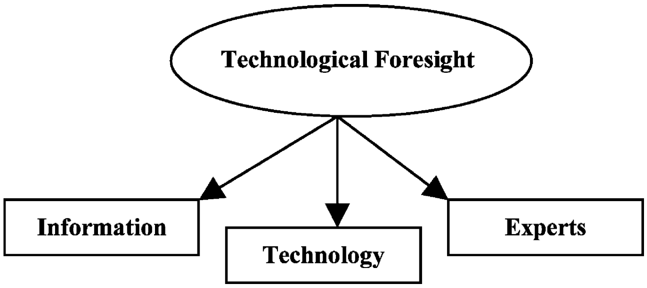
well as providing warnings about threats to be avoided in the globalized market.



According to Georghiu (2001), the applications of foresight currently in use are in their third generation and involve the participation of social stakeholders, as well as having a thematic agenda oriented towards the solution of socio-economic problems. This author emphasizes that some of the activities undertaken in this area, while initially focused on technology, end up producing recommendations which address the infrastructure of national systems of innovation.

2. The importance of knowledge and information management in technology foresight activities

Technological foresight has a common base in the retrieval and treatment of strategic information, the promotion and diffusion of analytical and reflexive skills, and the arriving at multiple interpretations. One cannot, however, obtain all the answers by means of foresight, nor expect to arrive at accurate predictions of the future. What is possible is to obtain glimpses of some tendencies or events which, with a greater or lesser degree of probability, may come to pass. These glimpses will provide indications of possibilities which may be attained through strategies and plans of action, as well as warnings about possible pitfalls.

According to Porter (1991), the importance of technology resides in its capacity to influence the structure of sectors and industries, altering the rules of competition, and opening opportunities for new players. This observation is in concordance with Schumpeter, who singles out the dynamics of technology and innovation as the only forces capable of creating appreciable changes in the market.

In the current climate of high uncertainty and hypercompetition, innovation has become part of the most important organizational strategies, an essential prerequisite to remaining competitive. Within companies, the processes of continuous learning and evaluation of internal competencies are being emphasized as complements to other methods of creating and maintaining competitive advantages. The value differential in organizations depends on their capacity to anticipate opportunities and threats, as well as their ability to capitalize on the tacit knowledge of their personnel. Intangible capitals, such as patents, know-how, intellectual capital and the promotion of network-based activities, tend to be more valued.

For Latour (2000), the diversity of actors and social relations involved in the production of knowledge creates relationships between them, creating what he calls socio-technical networks, which, in his model, favor the construction of scientific facts. These networks involve scientists and researchers, government and market agents and institutions. Inside these networks, the diversity of actors works to perfect ways and means of all kinds, increasing mobility, speed, reliability and the capacity to recombine among themselves.

Within this vision of the complex which is created around innovation, of the multiple agents and varied correlations which generate webs for the production of new wisdom destined to be used in the exploitation of new markets, appears the process of CI[1] as a decision-making support tool which seeks to reveal value-added information by means of the treatment, correlation and interpretation of large amounts of data obtained from different information sources.

The important conditions for the efficiency of CI are that it be based on the identification of user needs and that it be oriented to strategic necessities in the areas of information management, that is, the search for, selection and treatment of information of interest, in order to permit, amongst other possibilities, the visualization of trends and aids in decision-making. CI alone does not promote innovation, but it provides signposts for the flow of information which can be put into circulation to stimulate innovation.

2.1. *Patents and technological intelligence*

Patents are a significant factor in the creation of income from technology, principally in sectors which require large investments in R&D, such as the chemical–pharmaceutical industry (responsible for the launching on the market of active agents and formulations), and the biotechnology industry. Both these sectors, as well as being strongly science-intensive, are specialized suppliers, fitting into Bell and Pavitt's taxonomy as belonging to the category of firms which use patents as an important protection mechanism against imitation (Paviti, 1984).

[1] Competitive intelligence, although it has acquired new characteristics, methods and contributions (Fuld, 1995; Kahaner, 1996; Lesca, 1994; Canongia et al., 1999, 2002), has stimulated debate and evolution in areas within information systems, strategic planning and information technology. Competitive intelligence can be characterized as a set of activities which include the monitoring and analysis of data in both internal and external environments, with the goal of furnishing information which is useful in the business decision-making and strategic planning process (GESID, 1999).

Besides its important role in stimulating innovation, it should be emphasized that technological intelligence has shown itself to be an efficient tool in decision-making in the area of patents, bearing in mind its ability to permit identification of relevant technologies, partnerships, promising market niches, incremental innovation and competitor activity, as well as investments, process and product management, new R&D directions, potential mergers and acquisitions, amongst others. This approach is described by various authors in bibliography (Leydesdorff, 2001; Porter, 1998; Arsenova and Rozhkov, 1997; Wilson, 1987).

Leydesdorff, for example, has mapped the competitive arena of three drugs (Evista (raloxifene); Fosamax (alendronate); and Prozac (fluoxetine)), using patent databases, and has verified, using the citation curve, the correlation and applicability of these drugs, showing as well that one of them, developed for use in the treatment of osteoporosis, over a period of time came to be considered as for use in breast cancer regression (an anti-neoplastic agent), generating a new patent.

One factor to be emphasized is that using patents as an interesting information source for the generation of knowledge maps is aided by the fact that these databases are standardized, which allows for statistical treatment of the data with a low risk of error (Porter and Detampel, 1995).

The Brazilian Patent Office, INPI,[2] disseminates on the Web those patents issued since 1992; those issued previously require offline research. The patents of interest in the present study date from 1996, when a new patent law[3] eliminated the restriction of the previous law and permitted patenting in technological areas such as pharmaceuticals, medications, chemical and biotechnological products and food.

3. The potential of biotechnology in Health-care

One definition of *biotechnology*[4] which actors in the system of innovation, mainly academics and the press, agree on is that it is a conjunction of *enabling technologies* which have in common the use of biological cells or molecules applied in the production of goods and services in the areas of human and animal health, agriculture, energy and the environment (Pereira, 2002).

In order to produce a therapeutic biological substance, it is necessary not only to create a recombinant bacterium (genetic engineering), but also to master its multiplication (an industrial process related to fermentation) and the techniques of extraction and purification of the desired protein. In most cases, innovation takes place based on a combination of simpler techniques, from which emerges the combinatory nature of biotechnology (Batalha, 2000).

It is also worth noting that, internationally, this industry is characterized by technology-based companies, generally university spin-offs (SME) and by bioindustry (multinationals or transnational organizations). The IMS health report of 2000 notes the development of more than 1000 drugs for the treatment of cancer, of which 89% are biotechnology drugs.

Before delving deeper into the topic of this study, breast cancer, and as part of the foresight approach, a macrovision of the levels of business (markets), patents (technology) and scientific articles (R&D) is fundamental as a way of understanding the movement towards innovation. The following, therefore, presents reference tables which outline the potential of biotechnology in the area of healthcare.

- The biotechnology *market* has demonstrated growth and attractiveness, while at the same time has thrown up challenges to be found at the frontier of basic and technological knowledge. Bioindustry has been growing rapidly; in the USA, for example, the income it generated increased from US$ 8 billion in 1993 to US$ 20 billion in 1999, according to figures from Ernst and Young (2001). Indicators of international trends which show business opportunities demonstrate that the specialized ABI INFORM database has registered more than 1000 articles in the area of biotechnology in the last three years. The category of health, with 245 articles, was the most represented, followed by agriculture with 229 articles. Also identified were 107 more specific entries related to enzymes, molecular biology and genetic engineering.
- *Patents*, as indicators of innovation also demonstrate the potential of bioindustry in healthcare. At the beginning of this century (the period 2001–2002), for example, chronic cancer was responsible for the issue of 4282 patents based on biotechnology. This figure corresponds to around 40% of the total patents related to cancer, according to research undertaken in Derwents World Patents Index (WPI) database. Leadership is held by the USA followed by the UK.

[2] Instituto Nacional de Propriedade Industrial—http://www.inpi.gov.br/pesq_patentes/patentes.htm (Instituto Nacional de Propriedade Industrial, 2003).

[3] Law 9.279 on May 14, 1996.

[4] The terminology of biotechnology is vast, demonstrating its multi- and interdisciplinary nature: biotechnology; biogenesis; biomechanics; bioprosthesis; biodegradation; computational biology; bioethics; biopharmaceutics; biological assay; biological factors; molecular biology; biomedical technology; models biological; biological markers; biomedical engineering; receptors, biogenic amine; genes; genome; pharmacogenetics; genetics; genomics; genotype; genetic code; gene therapy; genes, rRNA; gene library; genome, genes, fungal; genome, human; genetic vectors; gene conversion; gene targeting; genes dominant; gene expression; genetic privacy; models genetic, amongst others.

- Technical-scientific production, that is, *articles*, reveals the extent of the explosion in biotechnology in healthcare. Research undertaken in the last two years (2001–2002) in the medical and related bibliographic reference database MEDLINE, reveals more than 30,000 articles on cancer (the diversity of types of cancer is high) and biotechnology, related to therapy, diagnosis or prevention. This shows the extent to which health research based on biotechnology has grown rapidly and fertilized discoveries fundamental to the improvement in quality of life. Leadership in cancer research is held by the USA, followed by the UK. Brazil, on the other hand, appears minimal in this area of activity.[5]

3.1. Why focus on breast cancer and biotechnology?

Among women worldwide, breast cancer appears as the second most common malignant neoplasm, as well as a significant cause of death from cancer. There do not exist any practical measures for primary prevention of breast cancer applicable to the population at large, although studies suggest that reductions in smoking, alcohol consumption, obesity and sedentary lifestyles reduce the risk of the disease. Technological advances have been aimed at early diagnosis and treatment, intended to increase survival rates (Parkin et al., 2002).

According to the American Cancer Society, in 2003, more than 266,000 women and 1300 men will be diagnosed as having breast cancer, and more than 39,000 women and 400 men will die from it. In the USA, breast cancer attacks one in 10 women, a fact which has stimulated R&D. The US National Cancer Institute (NCI), for example, has been testing 402 new cancer-fighting drugs, of which 59 are aimed at breast cancer.

As for R&D and innovation in the pharmaceutical industry, it has been shown that breast cancer has been the impetus for major initiatives, as cited by Alan F. Holmer of PhRMA (2001), who emphasizes the partnership of 170 pharmaceutical and biotechnology companies in the USA in the area of this chronic disease. It has also been noted with regard to R&D the pharmaceutical industry has been heavily influenced by the use of monoclonal antibodies[6] because these types of substances attack tumors exclusively, without causing many side effects, as they do not target normal cells, and thus offer better chances of recovery. In addition, drugs based on gene therapy have indicated new research avenues: the discovery of the gene C35, divulged at the latest annual cancer conference, was the result of research undertaken by the University of Rochester and the Vaccinex Inc. Company in partnership, and may represent an effective form of immunotherapy (Frank and Froelich, 2003).

In Brazil, both because of the increase in the number of cases diagnosed and the improvement in information about causes of death, a considerable increase in the mortality rate from breast cancer among women was observed between 1979 and 2000. This increased from 5.7 per 100,000 to 9.74 per 100,000, representing to an increase of 80.3%. The number of deaths and new cases among women expected in 2003 is 9335 and 41,610, respectively. These figures correspond to a death rate of 10.4 per 100,000 and an incidence rate of 46.35 per 100,00, respectively (INCA, 2003).

In spite of it being considered as a form of cancer with a relatively good prognosis if diagnosed early, the mortality rates for breast cancer continue to be high in Brazil, very likely because the illness continues to be diagnosed in advanced stages. Research based on the data available in hospital records shows that 60% of breast tumors, on average, are diagnosed in stage III or IV. Investment in technology and human resources within a program developed for early detection of this neoplasm, and the implementation of a national information system constitute important strategies which would change this scenario.

4. Breast cancer—methodology and foresight research

International data were collected in the area of health, using breast neoplasm or breast cancer as keywords in titles and abstracts, correlating these with the terminology characteristic of biotechnology in the 2001–2002 period. The sources of data used were:

- The international *MEDLINE* database, which provides complete coverage of world literature in the form of papers, books, journal articles, government reports, theses, company publications, congresses, conferences and patent registrations on a range of topics in the health area. One thousand and five hundred and fifty articles dealing specifically with therapy were recovered, in which it was possible to identify the most relevant countries, institutions, descriptors and substances, and, following analysis of the content of titles and abstracts, the value-added information presented in item IV.1 was created.
- The Derwent World Patents Index (WPI)—a global patents reference database. Three hundred and thirty patents were recovered and the most frequently occurring countries, companies or institutions assignees patents were indexed, based on an analysis of the content of titles and abstracts, providing an overview of trends in the 2001–2002 period.

[5] The results of research undertaken by the *Sistema de Informação sobre a Indústria Química* team (SIQUIM) of the EQ/UFRJ, for the Centro de Gestão e Estudos Estratégicos (CGEE), January 2003 (Sistema de Informação sobre a Indústria Química, 2003).

[6] Known as MAbs.

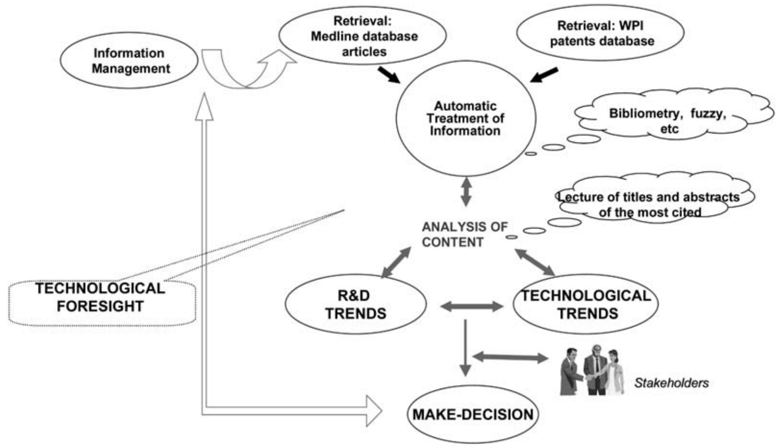


Fig. 1. Developed technological foresight methodology.

The results obtained from both databases were processed automatically, generating frequency lists, maps and reference tables, using, for example, Vantage Point software as an information and data and text mining[7] tool. The correlation of different variables is presented, allowing a decision-maker to globally visualize the movements and behaviors of the variables which are of interest. It should be noted that these tools are based on bibliometric algorithms, cluster analysis and fuzzy logic.

The overview generated by the automatic analysis was complemented by analyses of the content within the two information sources used. In the case of the articles, content analysis was undertaken by means of reading 60 titles and abstracts, representing the three top descriptors and the three most frequently cited substances, as well as 14 titles and abstracts written by authors affiliated to the institution with the highest frequency of publication. The 10 most frequent registrants of patents were identified, while in the content analysis, the titles and abstracts of 73 patents were analyzed, permitting the identification of not only the home country of the parent company, but also the visualization of trends in relation to these companies and their use of biotechnology in the fight against breast cancer.[8] The methodology is synthesized in Fig. 1.

[7] In the methodology used in this study, various approaches and software programs were used, amongst these was Vantage Point, developed by the Georgia Technology Institute—USA, which makes possible the creation of maps in which it is possible to show the most frequently cited substances, combinations of drugs, countries and institutions.

[8] This step in the organization and automatic processing of the data counted on the valuable collaboration of two interns in the *Sistema de Informação sobre a Indústria Química*—SIQUIM: Ana Carolina S. Mangueira (chemical engineering) and Max Arnor (statistics).

4.1. Results of foresight relation to the use of biotechnology in breast cancer-fighting drugs

With respect to technical-scientific production, the study identified those institutions with the highest frequency of articles published. Of the total of 1550 articles examined, the number of author institutions was 1262. The highest frequency of any one institution, 14, was obtained by the Department of Breast Medical Oncology at the University of Texas—M. D. Anderson. It should be noted that this same university also appears in second and third places, in the form of its Departments of Molecular and Cellular Oncology (five references) and of Surgical Oncology (four references). There are 63 institutions with a frequency higher than 2, and 1196 with a frequency of 1, demonstrating both a high degree of production and a high degree of diversity with regard to the locus of production. Table 1 presents the institutions with a frequency rate higher than 3 (12 in all), where the activity of universities, R&D centers and hospitals in breast cancer research is evident.

The USA also leads in the number of articles published (709), followed by England (250). Brazil does not appear in Fig. 2.

Analyzing keywords (mesh descriptors, that is, the controlled terminology in the indexation of the MEDLINE database) and substances, the following frequency results were obtained: of a total of 501 distinct descriptors, 346 represented a frequency equal to 1. Those with a frequency equal or greater than 10 (18 in all) are shown in Table 2.

It is possible to see the strong presence of articles on drugs for breast cancer treatment (comprising the first eight descriptors, plus the 12th and 15th). Of the 1550 articles considered, 345, or 22% relate to breast cancer treatment.

Analyzing the substances cited in the articles, the results make it possible to identify 1415 distinct sub-

Table 1
Leading institutions in scientific production related to the use of biotechnology in breast cancer treatment—2001 and 2002

Authoring institutions—articles on treatment	Number of articles
Department of Breast Medical Oncology, The University of Texas—M. D. Anderson, Texas, USA	14
Department of Molecular and Cellular Oncology, The University of Texas—M. D. Anderson, Texas, USA	5
Department of Surgical Oncology, The University of Texas—M. D. Anderson, Texas, USA	4
Blood and Marrow Transplant Service, Division of Hematology and Medical Oncology, Peter MacCallum Cancer Institute, Melbourne, Australia	3
Department of Biological Regulation, The Weizmann Institute of Science, Rehovot, Israel	3
Department of Medical Oncology, University General Hospital of Heraklion, Crete, Greece	3
Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, USA	3
Department of Medicine, Vanderbilt University School of Medicine, Nashville, USA	3
Department of Oncology, Lombardi Cancer Center, Georgetown University School of Medicine, Washington, USA	3
Department of Surgical Oncology, Osaka University Medical School, Osaka, Japan	3
Department of Surgery, Itami City Hospital, Japan	3
Investigational Drug Branch for Breast Cancer, European Organization for the Research and Treatment of Cancer Data Center, and Jules Bordet Institute, Brussels, Belgium	3

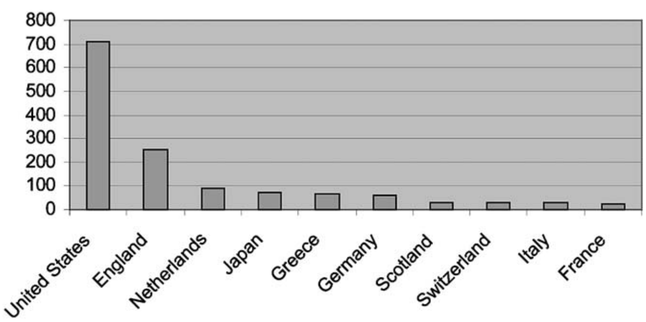


Fig. 2. Top-ranked countries in terms of publication of articles on breast cancer and biotechnology—2001 and 2002.

stances, with the highest frequency, 342, belonging to *Paclitaxel*. Eight hundred and sixteen substances show a frequency of 1, demonstrating the high degree of diversity of substances referred to in the articles. The 13 substances which present a frequency greater than 100 are shown in Table 3.

Supplementing the data analysis and text mining approach, analyses of the previously presented content were undertaken, by means of reading of the 60 titles and abstracts pertaining to the three most cited descriptors and substances, as well as the 14 pertaining to the institution with the highest frequency of publication. This permitted the identification of 23 drugs and/or drug combinations for the treatment of breast cancer. These are presented in Table 4.

Consultation in the index ABIQUIF (2003) shows that the single substance produced in the Mercosul area, amongst those presented in Table 4, is carboplatin (CAS—RN = 41575-94-4[9]; NCM=2843.90.00[10]), manufactured in Brazil by the Quiral Quimica company and in Argentina by Bio Sidus, Prosint and Desynth. This demonstrates the extent to which production of this type of drug is underdeveloped in the Mercosul area.

Table 2
Frequency of descriptors related to the use of biotechnology in breast cancer—2001 and 2002

Descriptors—focus: treatment	Number of articles
Breast neoplasms/*drug therapy	107
Breast neoplasms/*drug therapy/pathology	87
Breast neoplasms/drug therapy	41
Breast neoplasms/*drug therapy/metabolism	21
Breast neoplasms/drug therapy/*metabolism	18
Breast neoplasms/*drug therapy/metabolism/pathology	17
Breast neoplasms/*drug therapy/*pathology	15
Breast neoplasms/*drug therapy/mortality/pathology	14
Breast neoplasms/*therapy	14
Breast neoplasms/therapy	14
Breast neoplasms/*prevention and control	13
Breast neoplasms/drug therapy/*metabolism/pathology	13
Breast neoplasms/genetics/*prevention and control	13
Breast neoplasms/chemistry/*pathology/surgery	12
Breast neoplasms/drug therapy/metabolism	12
Breast neoplasms/*pathology	11
Breast neoplasms/*genetics/*prevention and control	10
Breast neoplasms/diagnosis/prevention and control	10

* The principal descriptor of the articles indexed in the MEDLINE.

The strong and weak points of the first five drugs and/or combinations in Table 4 are of utility to the different actors in the chain of production in the following ways: (a) *doctors* are able to follow new developments in order to find new possibilities of improving the quality of life of their patients, (b) *researchers* are able to more easily identify drugs and lines of research in potential partner institutions; (c) the *government* is able to prioritize investment in science-intensive therapies, and (d) *companies* are able to seek not only partners, but also develop strategies oriented to new therapies (Box 1).

Of the 330 patents related to breast cancer and biotechnology in the 2001–2002 period, 74 are in the area

9 The identifying number in the Chemical Abstracts Service.
10 Nomenclatura Comum Mercosul (Mercosul Common Nomenclature): a code which permits the identification of products as part of trade relations between countries and/or economic blocs.

Box 1
The strong and negative points of breast cancer therapies—2001 and 2002

- Trastuzumab + chemotherapy

  Strong: Gene therapy; increase in anti-tumor activity in HER 2/neu; increased rate of survival; trial in phases I, II, and III
  Weak: Ideal dosages and duration of drug administration unknown; cardiac dysfunction: high (trastuzumab + anthracycline + cyclophosphamide), medium (trastuzumab + paclitaxel), low (trastuzumab)
  Note: In the future, treatments will be customized for each patient

- Doxorubicin + taxanos (docetaxel or paclitaxel)

  Strong: Better results with doxorubicin+ docetaxel—anti-tumor efficiency; trials in phases I and II
  Weak: Higher cardiac effects with doxorubicin+ docetaxel than with doxorubicin + paclitaxel; doxorubicin + paclitaxel treatment is expensive; side effects with doxorubicin + docetaxel: nausea, vomiting, hair loss, neutropenia and mucositis
  Note: Treatment for advanced breast cancer

- Cationic liposome (E1A gene + DC-chol cationic liposome—DCC/E1A)

  Strong: Preclinical studies show repression of HER 2/neu; reversal of chain reaction; reduced proliferation
  Weak: Fever, nausea, vomiting
  Note: Breast and uterine cancer

- Vinorelbine + paclitaxel + G-CSF (granulocyte colony stimulation factor)

  Strong: Joint administration safe; high tolerance
  Weak: Fever, fatigue, myalgia
  Note: Phase II trial study recommended

- Vinorelbine + docetaxel + G-CSF

  Strong: Joint administration safe; greater synergy and anti-tumor activity
  Weak: Highly toxic, even in low dosages
  Note: Close monitoring of patients recommended

of diagnosis and therapy and 60 in the area of prevention, diagnosis and therapy. These two subgroups total more than half (154) of the patents analyzed using the data and text mining methodology, demonstrating the trend towards a wide scope of patenting, a value-added activity typical of the knowledge society. The tendency of these patents to be of value in the treatment of more than one illness, shown in Table 5, should also be noticed, as this increases available market niches and competitiveness.

Table 3
Frequency of citations of substances related to the use of biotechnology in breast cancer treatment—2001 and 2002

Name of therapeutic substance	Number of articles
Paclitaxel	342
Anti-neoplastic combined chemotherapy protocols	332
Anti-neoplastic agents	290
Receptor, erbB-2	245
Antibodies, monoclonal	183
Docetaxel	175
Tumor markers, biological	171
Anti-neoplastic agents, phytogenic	167
Trastuzumab	140
Doxorubicin	121
Receptors, estrogen	106
Tamoxifen	105
Cyclophosphamide	100

The title of the patent registration does not always contain a reference to cancer or to the application of the patent in prevention, diagnosis, treatment or drug combinations. This being the case, and in order to determine the relevance of the patent, it was necessary, in addition to data and text mining, to analyze the content, to look in the title and patent abstract for indications of the use of the drug and/or combination, as shown in Table 5. Amongst the patent registrants, the presence of partnerships between companies and individual inventors, as well as separate university initiatives should be noted. Also of note is the fact that, in addition to the various types of nomenclature (synonyms), in some situations, the text leaves the application implicit, as for example, "vaccine to prevent and/or search for a cure for breast cancer", implying application possibilities in the prevention of, as well as in the treatment of, breast cancer, subtleties which, even with the advances in artificial intelligence, are not brought to light automatically.

The 10 top patent registrants analyzed in the survey (nine companies and one university) are presented in Table 6.

The companies in Table 6 are distributed geographically as follows: seven in the USA, two in Japan, two in the UK (the Millenium company has a subsidiary in the UK). The US companies show a slight concentration in California. Of note is the diversity of registrants: of a total of 330 patents, only 32 present a frequency higher than 2.

Analysis of the 73 titles and abstracts of the 10 highest-ranked patent registrants demonstrates the macrotrends of these companies and institutions, illustrated in Box 2, revealing that the application in the area of

Box 2
Trends of the 10 highest-ranked registrants for breast cancer and biotechnology patents—2001 and 2002

- *Corixa Corp*.—proteins—breast tumors—prevention, diagnosis and prevention;
- *Incyte Genomics Inc*.—enzymes and cDNA—breast cancer, Alzheimer's, leukemia, AIDS, cardiovascular—prevention, diagnosis and therapy;
- *Diadexus Inc*.—genes and proteins—breast cancer—detection, monitoring, treatment (gene therapy);
- *Oxford Glycosciences UK Ltd*—protein detection (BCMP 7, BCMP 11 and BCMP 84)—breast cancer—screening, diagnosis, prognosis, prevention and treatment;
- *University of California*—diversified—antibodies and genes—breast and ovarian cancer—diagnosis, prognosis and treatment;
- *Isis Pharma Inc*.—oligonucleotides encoding casein kinase 2 (alpha or beta)—breast and prostate cancer—diagnosis and treatment;
- *Millenium Pharm Inc*.—polypeptides—cancer (breast, lung, ovary), Alzheimer's and Parkinson's, AIDS—diagnosis and treatment;
- *Bode Gene Dev Co. Ltd Shanghai*—hormones and polypeptides—breast cancer, AIDS, hypertension, arteriosclerosis—diagnosis and treatment;
- *Takeda Chem. Ind. Ltd*—G-protein—breast cancer, diabetes, respiratory illnesses—treatment and diagnosis;
- *Human Genome Sci. Inc*.—nucleic acids—breast cancer, cardiovascular, neurological illnesses—prevention, diagnosis and treatment.

more than one illness is a constant, with seven out of 10 companies presenting this characteristic.

5. Final considerations

The motivation for this study was the perception that Brazil has core competencies in biotechnology, as is shown in the following data: 1718 research groups, 6738 researchers and 16,174 students and interns; the country's bioindustry spans diverse economic sectors and corresponds to between 0.9% and 1.5% of the GDP (Gross Domestic Product); around 80 companies are active in the health sector; the number of deaths and new cases of breast cancer expected for the year 2003 amongst the Brazilian female population are 9335 and 41,610, respectively (SIQUIM, 2002).

This article presents evidence that foresight studies based on the methodology used here are of great value when employed in the development of R&D and innovation in scientific areas with social applications, as in the present case of biotechnology for the development of breast cancer drugs.

Based on the research undertaken, it is evident that technological foresight has a common base in the process of gathering and treatment of strategic information, the implementation of analytical and reflexive capacities, and the creation of multiple interpretations. The management of knowledge and that of information have shown themselves to be potent tools in supporting the decision-making process in the government, business, university R&D and research center environments, as well as in the medical and health professional field, providing value-added information, oriented to innovation, to be assimilated, interpreted and applied by these socio-technical actors.

Table 4
Drugs and/or drug combinations for the treatment of breast cancer—2001 and 2002

	Drug combinations		Drug combinations
1	Trastuzumab + Quimioterapia	13	Cyclophosphamide + thiotepa + carboplatin—CTC
2	Doxorubicin + taxanos (docetaxel ou paclitaxel)	14	Docetaxel + epirubicin
3	Liposome catiônico (E 1A gene + DC-chol cationic liposome—DCC/E1A)	15	Letrozole ("nonsteroidal aromatase inhibitor")
4	Vinorelbine + paclitaxel + G-CSF (granelocyte colony stimulation factor)	16	Paclitaxel + capecitabine
5	Vinorelbine + docetaxel + G-CSF	17	Cyclophosphamide + epirubicin + 5-fluorouracil—CEF + G-CSF
6	Eniluracil + 5-flourouracil + docetaxel	18	Gemcitabine + cyclophosphamide + 5-fluorouracil + Ácido fólico + G-CSF
7	Paclitaxel + 5-florouracil + adriamycin + cyclophosphamide—Pac/FAC	19	Mitoxantrone + cyclophosphamide com G-CSF + ciprofloxacin for hematological recovery
8	Paclitaxel + 5-florouracil + epirubicin + cyclophosphamide—Pac/FEC	20	Mitoxantrone + paclitaxel
9	ABI-007 (stabilized protein—monoparticulate of paclitaxel)	21	Protaxel
10	Docetaxel + trastuzumab	22	Angiogeneis
11	Gemcitabine + doxorubicin + paclitaxel	23	Raloxifene
12	Vaccine hemocyanin		–

Table 5
Breast cancer and biotechnology patents—2001 and 2002

Titles	Abstracts
Breast tumor proteins and nucleic acids useful for the prevention, diagnosis and treatment of breast cancer (patent registrant: Corixa Corp. and individual)	(...) USE—(I) and (II) may be used in the prevention, diagnosis and treatment of diseases associated with inappropriate BTP expression, i.e. breast tumors (...)
Novel human, mouse or rat resistin-like molecule, useful for treating and diagnosing irritable bowel disease, inflammatory bowel disease, diabetes, insulin resistance, obesity, syndrome X, colon cancer, breast cancer (patent registrant: Univ. Pennsylvania)	(...) USE—(...) (I) preferably, RELMalpha is useful for diagnosing insulin resistance and diabetes. (...) is useful for treating a disease mediated by malexpression of RELMalpha (e.g. breast cancer, tongue cancer, insulin resistance, diabetes, syndrome X or obesity) or RELMbeta (e.g. irritable bowel disease, inflammatory bowel disease, colon cancer, familial adenomatous polyposis or intestinal tumor) in a human
Nucleic acids encoding interleukin 17 receptor like polypeptides, useful for preventing, diagnosing and treating, e.g. leukemia, asthma, diabetes, psoriasis and glaucoma (patent registrant: AMGEN Inc. and individual)	(...) USE—(I) and (V) may be used in the prevention, diagnosis and treatment of diseases associated with inappropriate IL-17 receptor like polypeptide (IL17rlp) expression. Disorders that may be prevented, diagnosed and/or treated by the above methods include, for example immune disorders (e.g. inflammation, diabetes and transplant rejection), infections (e.g. hepatitis, septic shock and septicemia), weight disorders (e.g. anorexia, cachexia and obesity), neuronal dysfunction (e.g. Alzheimer's disease, Parkinson's disease and epilepsy), lung disorders (e.g. cystic fibrosis, asthma and emphysema), skin diseases (e.g. eczema and psoriasis), kidney disease (e.g. glomerulonephritis), bone diseases (e.g. osteoporosis, Paget's disease and hypocalcemia), vascular disorders (e.g. stroke, arteriosclerosis and restenosis), cancers (e.g. leukemia, myeloma and breast cancer), reproductive disorders (e.g. infertility and miscarriage), eye disorders (e.g. glaucoma and retinal neuropathy) (...)

Table 6
Ten most frequent breast cancer patent assignees—2001 and 2002

Patent assignee	Number of patents
Corixa Corp.[a]	12
Incyte Genomics Inc.[b]	11
Diadexus Inc.[c]	9
Oxford Glycosciences UK Ltd[d]	8
University of California[e]	7
Isis Pharma. Inc.[f]	7
Millenium Pharma. Inc.[g]	7
Bode Gene Dev. Co. Ltd, Shanghai[h]	6
Takeda Chem. Ind. Ltd[i]	6
Human Genome Inc.[j]	5

[a] Seattle, USA, www.corixa.com. "Corixa is a developer of immunotherapeutics with a commitment to treating and preventing autoimmune diseases, cancer and infectious diseases by understanding and directing the immune system."

[b] California, USA, www.incyte.com. Incyte is a "drug discovery company applying its expertise in genomics, medicinal chemistry and molecular, cellular and in vivo biology to the discovery and development of novel small molecule and protein therapeutics".

[c] California, USA, www.diadexus.com. Diadexus Inc. is "a privately held biotechnology company, is focused on the discovery, development, and commercialization of novel, patent protected diagnostic and therapeutic products with high clinical value".

[d] Oxford, UK, www.ogs.com. Oxford Glycosciences UK Ltd is a biopharmaceutical company where the first proteomics lab in the world was created. At this lab, many kinds of proteins—amino acids—have been discovered through image analysis and sequence databases.

[e] California, USA, www.berkeley.edu. Graduate program in computational and genomic biology.

[f] Alpharma Inc., USA, is a growing specialty pharmaceutical company which bought Schwarz Pharma (a German company), including Isis Pharma—www.isispharma.de.

[g] USA and UK, www.mlnm.com. Applies genomics in the development of life-science-based products and services. The goal is to use deep understanding of mechanisms and pathways of disease together with the unique characteristics of the individual to accelerate the prevention, detection and cure of disease. This is an approach called personalized medicine.

[h] Shanghai, China. Shanghai Bode Gene Development Co. Ltd merged with Guangdong Zhaoqing Star Lake Biological Science & Technology Co. Ltd in the end of August 2000, to form the largest biochip company in China. Shanghai Bode Gene Co. uses its biochip technology to evaluate its shares. It is reported that Shanghai Bode Gene Co. has applied for over 2000 patents for gene pharmaceuticals.

[i] Tokyo, Japan, www.takeda.co.jp. Takeda is a research-based global company with its main focus on pharmaceuticals. It is the largest pharmaceutical company in Japan and is among the leaders in the world. Takeda discovers, develops, manufactures and markets a broad range of superior pharmaceutical products to improve the health and quality of life of people around the world.

[j] Maryland, USA, www.hgsi.com. Human Genome Sciences Inc., is a pioneer in genomics for the discovery and development of new pharmaceutical products. Its goal is to become a global biopharmaceutical company that discovers, develops, manufactures and sells its own gene-based drugs.

Biotechnology brings the promise of new scenarios for the 21st century in various economic sectors, especially health, providing new techniques and drugs for the treatment of, amongst other chronic illnesses, cancer, and in particular, the focus of this study, breast cancer. It has been demonstrated that the USA concentrates on both the technical-scientific production and patent registry in this area, followed by the UK and Japan. Also demonstrated were the cooperative efforts between different actors in the production of both research articles and patents.

The international trends observed in relation to the use of biotechnology for breast cancer drugs are in the direction of prevention (vaccines), diagnosis (biological markers) and treatment (23 drugs and drug combinations stand out as the main therapies, with the drug paclitaxel being the most cited). The importance of clinical research has been underlined, as being essential in the process of innovation, based on the goal of increasing survival rates of cancer sufferers and of minimizing the weak points of each form of therapy.

The articles and patents recommend and reinforce the necessity of early diagnosis in attaining the goal of a cure with no reincidence within a five-year period. On the prevention front, thanks to biotechnological advances in vaccines (using genes specific to breast cancer as *antigenes*), a range of possibilities are opening up, which promises to bring progress in dealing with the currently alarming rates for this illness. On the treatment front, the results of data mining bring to light more efficient possibilities, with fewer toxic effects, depending on the stage of the illness.

Finally, it is important to emphasize the importance of the network of social actors (stakeholders) in the process of the exchange, analysis and use of this knowledge, which increases the synergy between government, academia, business, NGOs, doctors and hospitals, thus feeding the competition and innovation within the breast cancer treatment productive chain.

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