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Knowledge Management Trends in Biotechnology in Brazil

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Abstract

This chapter presents a study on knowledge management and innovation in biotechnology area through analysis of scientific and technological advances of biotechnology trends in Brazil, providing an overview of the science profile as well as regional development and its relation to issues on topics based on the analysis of scientific publications for the last 20 years. Given these promising prospects, the monitoring and searching of scientific advances and trends in this area of knowledge have become essential for searching opportunities in research and development and also for potential innovations and business opportunities, both in the developed countries as well as in countries of emerging economies such as Brazil. The research was realized using database Web of Science with 60 terms selected in Biotechnology area and 73,125 documents have been organized. Scientific indicators were produced using data/text mining tools. A greater number of scientific publications were found in areas such as biochemistry and molecular biology; genetics and heredity showing a greater frequency in these terms: vaccine, PCR, and genome. Results pointed out the US as the main foreign partner-country of scientific publications followed by the UK, France, and Germany. It was possible to verify cooperation network with others Latin American countries.

Keywords: knowledge management, innovation, scientific trends, biotechnology, Brazil

1. Introduction

Technological advancement has been the dominant driving force in modern society leading to a widespread diffusion of products from the rational activity as well as of scientific, technological, and administrative sources, which in turn requires new types of management [1].

This technological progress has induced a new paradigm based on the development of a set of intensive knowledge on scientific technologies, which represent many applications of scientific discoveries, whose core is to develop an increasing competence to manage information and knowledge. In this contemporary setting, the intangibles assets such as knowledge (know how), patents, and intellectual capital become increasing value strategic elements to be the center of contemporary forms of capital accumulation [2].

Biotechnology as a highly scientific sector is one of the most knowledge-intensive activities in the contemporary economy, having a direct and indirect impact on regional and national economies. The phenomenon of growth in the production of biotechnological products is relatively new, and in the long term, the growth potential is probably associated with the greater diffusion and use of your products and processes due to its convergence with nanotechnologies, information technologies, and other applied sciences [3].

In this context, biotechnology is considered as one of the most important technological tools nowadays. It is considered a key "future-bearing technology" and its applications have contributed to the structuring of new economic and social systems [4]. In this sense, biotechnology appears to have the characteristics of a core technology, with the potential to underpin a new technoeconomic paradigm.

Biotechnology represents a set of technologies "that use biological systems, living organisms, or their derivatives to produce or modify products and processes for a specific use" [5]. Biotechnology features a multidimensional nature, involving different knowledges, scientific and technological. Indeed, biotechnology can be considered as the result of a scientific revolution that involves many disciplines. In other words, it is a "constellation of scientific revolutions" [6], which is based on different areas of knowledge such as molecular biology, biochemistry, computer science, biophysics, engineering, and others.

The large set of biotechnological methods along with its different forms of application results in different interpretations about the dimensions that compose the biotechnology [7]. It has helped to generate new high-impact services in various segments such as health area with impressive revolution in the treatment of diseases as well as the use of new drugs for humans. It is also possible to verify its impact on agriculture with the development of functional foods and the reproduction of plant species; in the chemical and petrochemical industries with treatments of wastes and wastewaters; and the sustainable use of biodiversity, among other areas [2].

When assessing the potential application of modern biotechnology for the next 20 years, some authors assert that areas such as genomics, proteomics (spatial identification of protein structures), biomaterials, bioengineering, pharmacogenomics, genetic engineering, genetically modified foods, and synthetic biology will have a great impact on the future [2, 8].

In view of these future prospects, the monitoring and research of scientific advances and trends in this area of knowledge have become essential for searching opportunities in research and development (R&D), as well as for potential innovations and business opportunities, in the developed countries and mainly in countries of emerging economies such as Brazil [2]. Countries with rich biodiversity, mainly South American countries such as Brazil and Colombia, have tried to develop national capacities in science and technology (through

improving their infrastructure, greater participation in network experts, training of human resources, the increase publications) that allows a better optimization of scientific resources and economics and the generation of technological products based on nationally developed biotechnology [2, 9].

In this situational scenario, in order to propose worldwide profile of knowledge management of trends in biotechnology in Brazil, this chapter presents science trends in this area, mapped out through a set of variables such as the identification of the actors involved as well as the institutional partnerships, the major journals, among others, using the analysis of all Brazilian scientific publications of international dissemination for the period of 1995–2014.

2. Biotechnology in the global market and Brazilian government programs

2.1. Biotechnology in the global market

For centuries, humans have used biotechnology in their daily lives. Biotechnology presents as the growth area and development products and technologies observed in different areas of economy, which use live microorganisms or parts of them [10], showing up as a promising area among the diverse emerging technological developments. Being a multidisciplinary area presents the possibility of new products and processes. The bioindustry has contributed to the economic and social growth by bringing new solutions to problems concerning to human and animal health, to agribusiness, the environment, and the creation of new materials. In these aspects, biotechnology is a technological innovation that also provides products or processes with social or commercial use [11].

As technological progress advances based on life sciences, the possibilities of obtaining products with higher added value or lower production costs increase. The most prospected areas of biotechnology are health (pharmaceutical) and agriculture (food) [2]. On the economic bias, biotechnology is a major focus of activities on research, development, and innovation in the developed countries and it is becoming increasingly central in developing countries due to the potential of exploiting great biodiversity [12].

For a long time, it has been emphasized about the biotechnology potential and the future full of innovations that it provides. However, today, we can observe that the largest potential innovators are in the United States and Europe (the United Kingdom, Germany, and France). Due to their investments in the chemical and pharmaceutical corporations they become owner of biotechnology companies, enlarge their capabilities of innovation, or maximized new products generation [13].

The biotechnology industry has been grown rapidly in recent years, more than doubled its worldwide revenue in the last decade, going from US$ 8 billion in 1993 to US$ 20 billion in 1999 [14]. According to the study presented in Ref. [15], the worldwide market for biotechnology resources moves expressive values of about $ 410 billion per year. The worldwide market

for biotechnology between 2002 and 2006 grew at a compound annual growth rate (CAGR) of 13.4% [16]. Figures in this market are not very consistent. According to the study presented in Ref. [17], the United States alone moved the biotechnology industry resources of US$ 3.7 billion in 2009, being the market that moves much capital in this biotechnology market.

Regarding innovative effort, we can affirm that the United States is the country that spent more on R&D in biotechnology. In 2009, it spent only in entrepreneurial sector, US$ 22 billion on R&D, followed by France, Germany, and Canada, with the total expense on R&D about US$ 2.5, 1.3, and 1 billion, respectively [18].

In Asia and Pacific, among the countries that are more prominent, Japan is the most advanced in the biotechnology area, due mainly to the cooperation work developed by Japanese government, universities and private sector, directed especially to build an adequate infrastructure for innovative business *start-ups* [18]. After that the focus turns on Singapore, Taiwan, China, India, and Australia. The Chinese government, for example, invested about US$ 40 billion in the biotechnology industry in 2012 and, the Singapore government hopes to increase 20% biotechnology investments in the next 5 years, that is, it is intended to spend about US$ 12.5 billion in R&D in this sector [18].

2.2. Biotechnology in Brazilian government programs

The biotechnology segment holds a special place among the priorities at government policies, as much for the developed country and as for developing countries. The wide set of opportunities created by biotechnology, especially in health and agriculture areas, show the essentiality of its development as competitive strategy and expansion input in international market, mainly in developing countries such as Brazil. Brazil is a country with great potential for the development of agricultural biotechnology because it has a wide biological diversity and is rich in plants, animals, and microorganisms [19]. Since the 1970s, the biotechnology applied in agriculture has been productive and economic relevance in the country.

This chapter focuses on the characteristics and development of biotechnology in Brazil and refers to the public investment, with the main aspects of the most noteworthy programs and financing structure. There is a governmental structure in the country directed for the development of the area. This structure is composed of the following ministries: the Ministry of Science, Technology and Innovation (MST&I); Environment and Agriculture; Production and Trade; and Health and Social Development. At the same time, the government also acts through its government agencies, the private sector, and academia [2].

The government policies to support the development and financing on biotechnology in Brazil have started since 1980 with the promotion of several programs dedicated to the area, the Integrated Genetic Program, which aimed at introducing some specific actions on genetic engineering. In 1981, the government officially unveiled the National Program for Biotechnology (Pronab) which was to consolidate public investments for maintenance of the research groups in areas related to the program.

In 1984, the Ministry of Science and Technology (MST) had created a wide program in order to support, finance, and develop strategic areas in the country. This program was the development

support to Scientific and Technological Program (PADCT), cofinanced by International Bank for Reconstruction and Development (BIRD). Since its beginning, biotechnology has been seen as a strategic area for the scientific development in the country and, thus, established a specific subprogram to support it, the Biotechnology Subprogram (SBIO). PADCT started in 1985 and its actions were continued until the 2000s. At first, PADCT prioritized the development of some activities such as molecular biology, genetic engineering, and biosafety, without forgetting areas such as biochemistry, microbiology, and agronomy.

From the wide vision, PADCT aimed to build physical structures for research centers and development projects in cooperation in order to attract private investment, promote dissemination, and technology transfer from academic centers to the production sector. During this period, the first biotech products emerged that were human insulin, biodegradable plastics, biofilm, genetically modified plants, among others.

Early in the 1990s, both the government and the private sector have reduced the resources applied to biotechnology due to low commercial return of biotech products developed so far.

In 1999, the government changed the pathway of financing in Brazil through the creation of sources of fiscal financing from various economic sectors, called sectoral funds. In 2001, the biotechnology sector fund was created and its main objective was to ensure the continuity of biotechnology research, especially those considered as strategic for the country. Somehow, the creation of Biotech fund strengthens the National Program of Biotechnology and Genetic, established in 2000 and under MST&I responsibility. The program emphasized actions to "conservation genetic resources and development of biotechnological products and processes with applications in industries, agriculture, and human health". Several of these opportunities have been adopted as strategy of the project management in networking way in order to increase the flow of innovation and the results to society.

Among the many action plans applied from 2002, it is worth mentioning the following: Brazilian Genome Project, Structural Biology Network, Brazilian Proteomics Network, the development of biopharmaceuticals and immunobiology, and the development of new technological routes.

In 2004, the government using the Brazil's Industrial, Technological and Foreign Trade Policy (PITCE) pointed out biotechnology as the "future-bearing technology." On that political occasion, the Biotechnology Competitiveness Forum had created in order to put together all actors involved in the production chain in favor of strengthening industrial competitiveness.

Biotechnology research is funded by federal, private, and international agencies. The Organic Law of Science, Technology and Innovation (Decree No. 10.973 of 2/12/2004) defines some coordination organizations on the national level, and the Ministry for Science, Technology and Innovation (MST&I) represents the leading national organization [2].

From Biotechnology Competitiveness Forum, in 2007, begun the Biotechnology Development Policy (PDB), which established the National Biotechnology Committee (CNB). On the whole policy, structuring actions were defined in order to promote transfer of technology, investments, training of human resources, strengthen networks, regulatory framework, and to improve infrastructure for research centers and R&D. Examples of priority areas supported

were: plant and animal breeding, food technology, bioinformatics and immunology, diagnosis and prospecting on biotechnology, and detection of genetically modified organisms.

3. Methodology and recovery documents

3.1. Database

The research was based on the selection of scientific publications collected in ISI/Web of Knowledge[SM] database. It is international bibliographic data and is used as reference for the generation of indicators of S&T and Innovation [2].

3.2. Strategies for recovery documents

The strategy for the recovery of publications on a particular scientific topic must be carried out carefully to avoid damaging in the analysis of scientific literature. For the analysis of results in an accurate overview of the subject, ideally, the "search expression" must promote the recovery of all relevant publications on the subject present in the database, and at the same time, exclude nonrelevant publications. However, such situation is difficult to achieve since the multidisciplinary issues receive contributions from several areas of knowledge.

The solution for recovery of significant and coherent set of publications that allows an analysis of the scientific production in the biotechnology area was the elaboration of a complex search expression, consisting a large of set selected and tested keywords.

At first, we tried to develop search strategies in the mode "ISI-general search," using keywords from the available literature and descriptors present on the *Platform-Lattes*/National Council for Scientific and Technological Development (CNPq) - Brazil and *Portal Innovation*/MSCT-Brazil related to research groups and ongoing research in the biotechnology area. These search expressions were just an exploratory character, that is, serve as a basis for elaborate more refined expressions and evaluate how the area is organized into database [20]. A selection from bibliographic references was also used.

In order to achieve the purpose of mining scientific production on biotechnology in Brazil over a period of 21 years (1995–2015), 60 distinct descriptors (**Table 1**) were used, selected by experts in biotechnology area, interviewed and research groups in the biotechnology area sought in the base *Plataforma Lattes CNPq/Brazil* and *Portal Innovation*/MSCT-Brazil.

From our previous experiences, we found that the best way to do this recovery would be a combination of different expressions. For this, we used the advanced search mode of ISI/Web of Science and the advanced search. Once defined the strategy, we used all these keywords, and various search expression and their combinations in the database ISI/Web of Science only looking for indexed publication using document types "article." The fields "Title, Summary, and Keyword" were used to analyze the themes of scientific publications with international dissemination [21].

Antisense	Biomaterial	Proteins engineering	GMO
Recombinant antigen	Biopolymer	Genetic engineering	Protein
Biodiversity	Bioprocess	Metabolic engineering	Recombinant protein
Biocatalyst	Bioprospection	Molecular engineering	Proteome
Biofuel	Bioreactor	Gene expression	Proteomic
Bioeconomy	Bioremediation	Pharmacogenomics	PCR
Bioengineering	Biosensor	Phytoremediation	RNA
Bioethics	Biosorption	Gene	Microarray DNA
Biofiltration	Biosurfactant	Genetic	Microarray RNA
Bioindustry	Biosulfurization	Genome	Transcriptome
Bioinformatics	Biotechnology	Genomic	Transgenic
Biolixiviation	Stem cells	Microbiota	Cellular therapy
Computational biology	Cloning	Biology modeling	Gene therapy
Biome	T cells	Nanobiotechnology	Molecular therapy
Biomass	DNA	Peptide	Vaccine

Table 1. Biotechnology-related terms used to search articles in database ISI/Web of Science.

The software VantagePoint® was used to perform the processing of information from articles retrieved in order to expand and enrich the results. VantagePoint® allows management of big data and information in order to present correlations of distinct variables of interest. It also allows us to identify Who, What, When, and Where, help us clarify relationships and find critical patterns, among other possibilities [2].

For visualization of the data, we used the software VOSviewer®. It is a latest free software for the representation and analysis of information, which appears as an alternative to the traditional techniques of multidimensional representation and network display. VOSviewer combines the visualization and clustering techniques, favoring analysis while bypassing unnecessary technical complications. It make possible to view the maps of collaboration between institutions, countries, and keywords [22].

After this step, macroindicators were generated for providing a global overview of the scientific production on biotechnology in Brazil and raising the main issues as follows: (1) the total number of articles published per year (1995/2015) and the trend of publication of the most frequently used terms; (2) major journals that institutions often publish their articles in this specific area; (3) key areas of knowledge and the number of articles published on the used terms; and (4) the number of papers published by institutions and maps of network (institutions and countries) for the purpose of identifying partnership [2].

The trends for biotechnology were mapped out through a set of variables such as the identification of the actors involved as well as the institutional partnerships and networking.

4. Overview of the global scientific development in biotechnology in Brazil

4.1. Analysis of results and cowords networks

Government policies to incentive and promote R&D activities in biotechnology in Brazil have started since the 1980s. However, from the late 1990s and the early 2000s, especially in 2001, with the creation of the national fund for biotechnology, the area aimed at real conditions of productivity and competitiveness in R&D. Biotechnology has its amended financing path taking up considerable resources of 97% between 2002 and 2003, with the resources allocation from the National Fund for Scientific and Technological/FNDCT, managed by the MSCT, CNPq, and Studies and Projects Financing Institution (FINEP) [23].

From the data collected in the ISI database, bibliometric indicators have been produced that will help us to understand the scientific activity in the biotechnology area.

With regard to the scientific literature on biotechnology for the period between 1995 and 2015, it was retrieved 102,326 documents containing terms selected by experts in the fields of title, abstract, and keywords, and 69,977 documents where Brazil as the home country (1st author). **Figure 1** shows the evolution of publication number in biotechnology area since 1995.

By analysis, the number of articles published throughout this period was possible to observe that there is an increase in publication trends, which indicates an intensive scientific activity over the past 15 years, mainly in the last 8 years. An exponential growth with increased production greater than 6500% was observed, as shown in **Figure 1**. However, this scenario
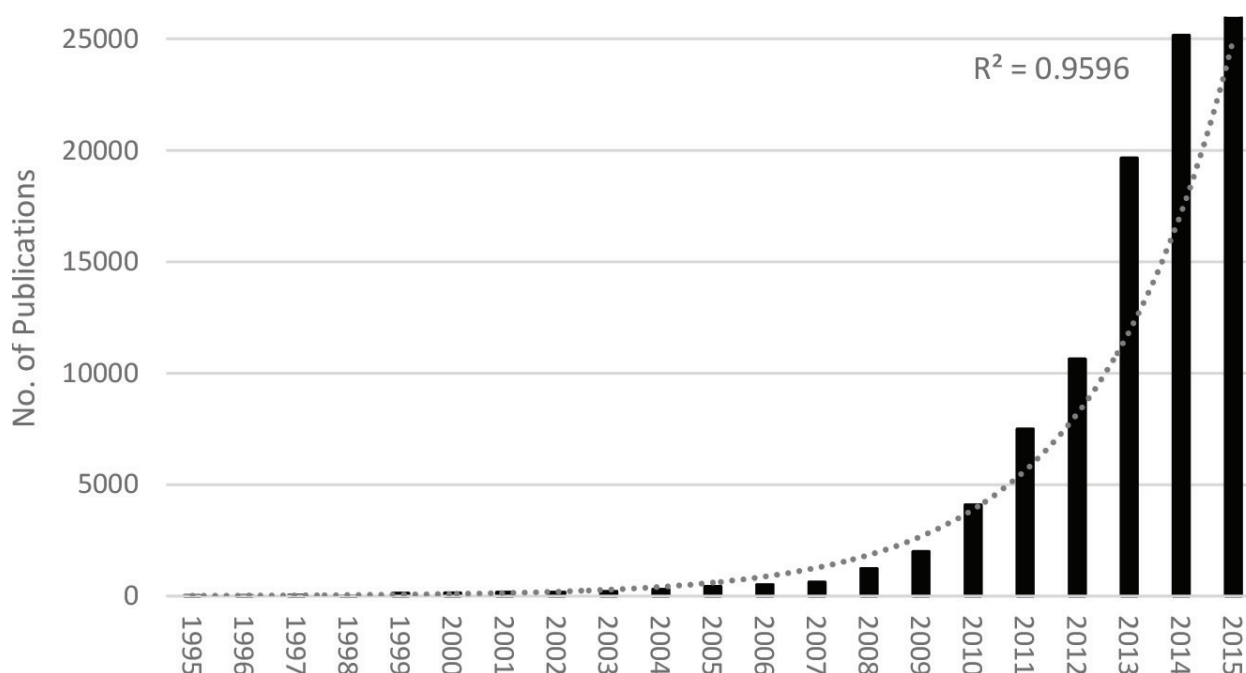

Figure 1. Historical evolution of biotechnology scientific publishing indexed in Brazil since 1995.

of accelerated growth should be modified in the coming years because of the reduction of R&D investments by government agencies in recent two years (2014–2016); due to the severe economic crisis that Brazil has been facing since 2013, which will reflect in a slowdown of the scientific production in the country for the next years.

A probable cause of this growth seems to be the key role that the activities of biotechnology have gained notoriety on a worldwide scale in recent decades. In Brazil, this increase observed reflects the research government incentives, established the financial investments in the area and the implementation of government policies, as aforementioned.

With respect to the most frequently used terms to screen the biotechnology area in Brazil, it was possible to find a large dispersion in relation to them [2], which means that there are more than 7000 distinct descriptors (keywords) described by the authors in the scientific publications as examples: Vaccine, PCR, DNA, Genome, Leishmania, *Trypanosoma cruzi*, HIV, among others. Some of them were not used as initial descriptors when searching the database.

In the specific evaluation of these terms, we noted that terms such as DNA and PCR are often used since the beginning of the period analyzed, which means that since 1998, these are being associated with modern biotechnology techniques [2]. Other terms such as "genomic," (72 articles) "proteomics," (32 articles), and "stem cell" (37 articles) are further frequent, however, they are related to more advanced future-bearing technologies of modern biotechnology, being mentioned in Brazil by the National Biotechnology Committee as the frontier areas of biotechnology. This observed result is associated with the Brazil collaboration in the genome projects, as example the mapping of the *Xylella fastidiosa* genome in 1997, and later, working in international project such as Human Genome Project (HGP) in 1999. *X. fastidiosa* is a bacterium that attacks citrus agriculture producing "little yellow" and decreasing agricultural productivity, so this project was essential for the control of this pest in Brazilian farming. This project was much important because it was the first phytopathogen sequenced in the world.

According to Santana et al. [2] and Pisano [6], some areas of biotechnology will have a significant impact in the near future on the development of new technologies and its applications, which are the genomics, pharmacogenomics, transcriptomics, biomaterials, bioengineering, and synthetic biology. Some themes related to these terms were detected in this dataset. **Table 2** presents the terms mentioned by the authors (keywords' author) with more than 50 citations related to the field of biotechnology.

From the total of scientific publications found, it can be observed the terms like *Leishmania*, *T. cruzi*, *Schistosoma mansoni*, and Chagas disease, which refer to a potential application. It should be emphasized that the data collected point out that scientific research on biotechnology in Brazil is directly related to the study of some relevant social problems of a country mainly related to tropical diseases.

Neglected tropical disease (NTD) has become an extremely important issue in public health in Brazil, as they profoundly affect the quality of life and generate negative socioeconomic impacts for the population of the poorest countries. Although not unique to developing countries, they arouse little financial appeal from the large pharmaceutical industry, since they do not reach the large consumer market that is the developed countries. In Brazil, the

Articles	Top terms (keywords)	Articles	Top terms (keywords)	Articles	Top terms (keywords)
380	Vaccines	99	Cell	71	Molecular marker
324	PCR	83	Diagnosis	69	gene
232	DNA	82	Expressed gene	65	HIV
183	Genetic	85	Genotype	64	Microsatellite
134	Brazil	79	*Trypanosoma cruzi*	66	Chromosome
120	Genome	78	Oxidative stress	61	Apoptosis
115	Polymorphic	75	Cytokine	63	Bovine diseases
131	Leishmania	72	Genomics	57	Cancer
56	*Schistosoma mansoni*	56	Inflammation	54	Fish
54	Chagas disease	53	Epidemiology	50	Drugs

Table 2. Terms with more than 50 citations used by authors in the fields title, abstract and keywords in the articles published by Brazil.

Ministries of Health, Science and Technology and the Health Surveillance Secretariat defined seven neglected tropical diseases based on epidemiological criteria, disease impact, and demographic data. They are dengue, Chagas disease, leishmaniasis, malaria, schistosomiasis, leprosy, and tuberculosis [24].

Figure 2 presents a network map where the main lines of research stand out. This map representation was obtained using VOSviewer®, taking as the matrix of cooccurrence of the 7000 keywords' and authors standardized by the measure of strength of association [21].

Although the keywords, which represent the domain of cells and genome, show a highly interrelated distribution, the structure can be clearly seen. Analysis of the relations among the most frequent descriptors reveals four well-defined groups, but with a variable degree of dispersion. In the upper part (1), around the nodes infection and vaccine, we find the most compact group of the network. It includes descriptors that represent documents in the areas of immunology, infectious diseases, and tropical medicine, related fundamentally with the application and clinical research into tropical diseases.

This scenario is compounded by the lack of innovation in drug R&D programs in the area of NTD; thus, the situation requires a concentrated global for the creation and maintenance of R&D programs focused on the discovery of new alternative therapies for the control and treatment of these diseases [25, 26]. Modern biotechnological tools (e.g., genomics, functional genomics, proteomics, metabolomics, and cytometry) have provided valuable insights for the discovery and development of new drugs that are extremely useful in coping with these NTDs. Extremely important initiatives are being successfully implemented to include Brazil in an increasingly significant science and technology scenario. According to Guido et al. [25, 26], three examples are presented to illustrate the breadth and diversity of networks and partnerships that have provided great opportunities and challenges in the area of NTD.
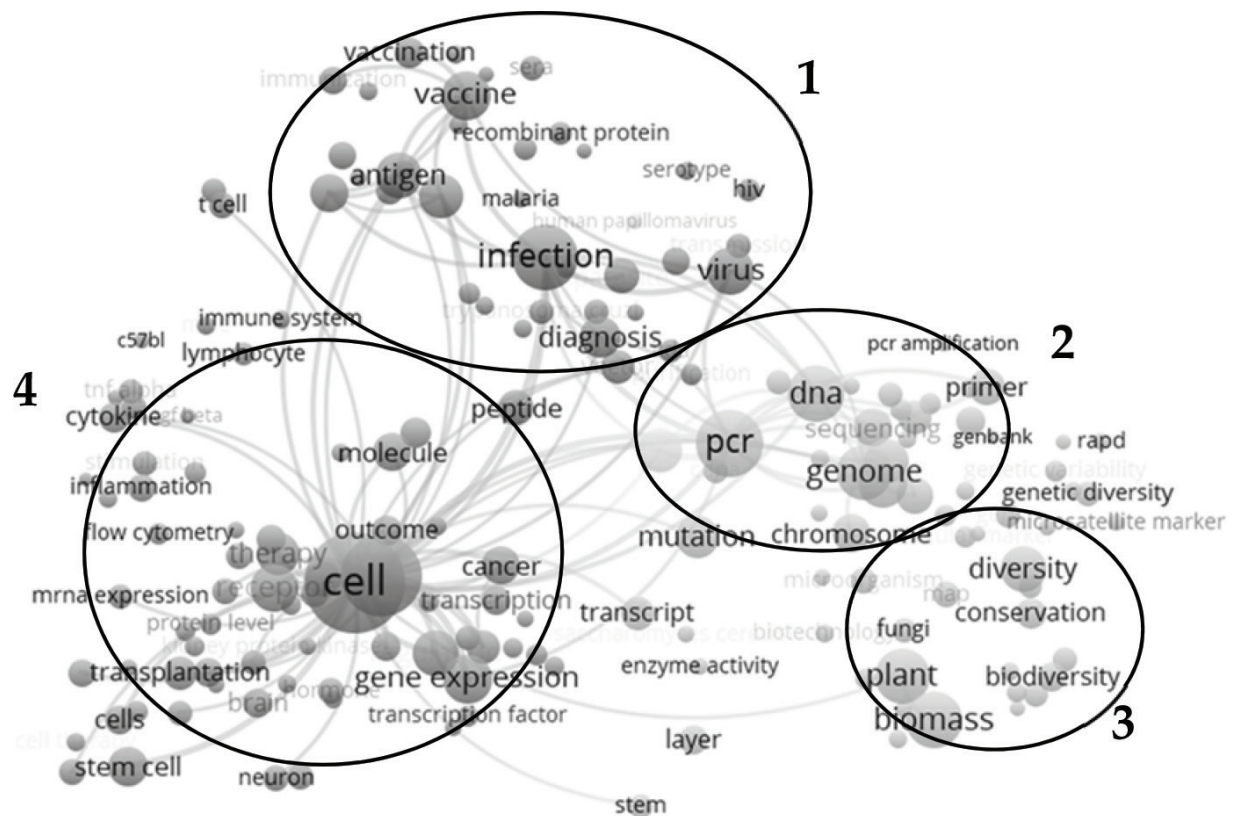
Figure 2. Map of keywords based on a co-occurrence network on biotechnology in Brazil. *Source*: Map presentation software VOSviewer®.

To the right, cluster 2, the keywords genome, PCR, and DNA connect with a well-defined cluster of descriptors related to genetics, and molecular biology research related fundamentally with the application and clinical research into the genome of *X. fastidiosa* begun in the 1990s.

Genomics is also closely related to agriculture not only in genetic improvement of species such as transgenic crops (with resistance to pests and tolerance to pesticides), but also in the product quality changes (plants that produce hormone, eucalyptus with higher production cellulose). More recently, Brazil has been developing research on feasibility of plants, animals, and microorganisms as biofactories of molecules of agricultural, pharmaceutical and industrial interest; identification and applications of genes and biological functions that promote tolerance to abiotic and biotic stresses and elimination of contaminants in food; identification and characterization (structural and functional) of new molecules to increase the production capacity of biologically based products with low environmental impact; and identification and applications of genes and biological functions that promote tolerance to abiotic and biotic stresses and elimination of contaminants in food [27].

Meanwhile, the terms of biomass, diversity, and conversation compose the third cluster 3, far right, including areas of biotechnology and biodiversity. To the left, cluster 4, we have the keywords (cell, gene expression, and stem cell) associated with molecular biology and cell biology areas related to the processes of modern biotechnology associated with a medicine, oncology, and neuroscience therapies.

The information obtained through keywords analysis is much more comprehensive and precise. For this reason, even though the two largely coincide or overlap, subject categories (see **Figure 3**) are more general or superficial than the information based on keywords (**Figure 2**). The latter shows, with a greater level of desegregation, the distribution of the descriptors that specifically configure each thematic profile, plus the less productive or incipient research that would otherwise remain hidden [28].

4.2. Profile of the scientific sector: biotechnology

By its intrinsic multidisciplinary characteristics, biotechnology permeates many areas of knowledge. Therefore, when analyzing the frequency of publication of scientific areas, there is a predominance of biochemistry and molecular Biology (12.4%), followed by genetics and heredity (10.94%), immunology (8.66%), microbiology (7.57%), and veterinary science (6.22%) together representing 45.79% of total articles published. However, this study highlights the wide dispersion of scientific publications by all thematic areas. **Figure 3** demonstrates the percentage distribution for all the 20 areas with the number of articles greater than 200 indexed in ISI/Web of Science.
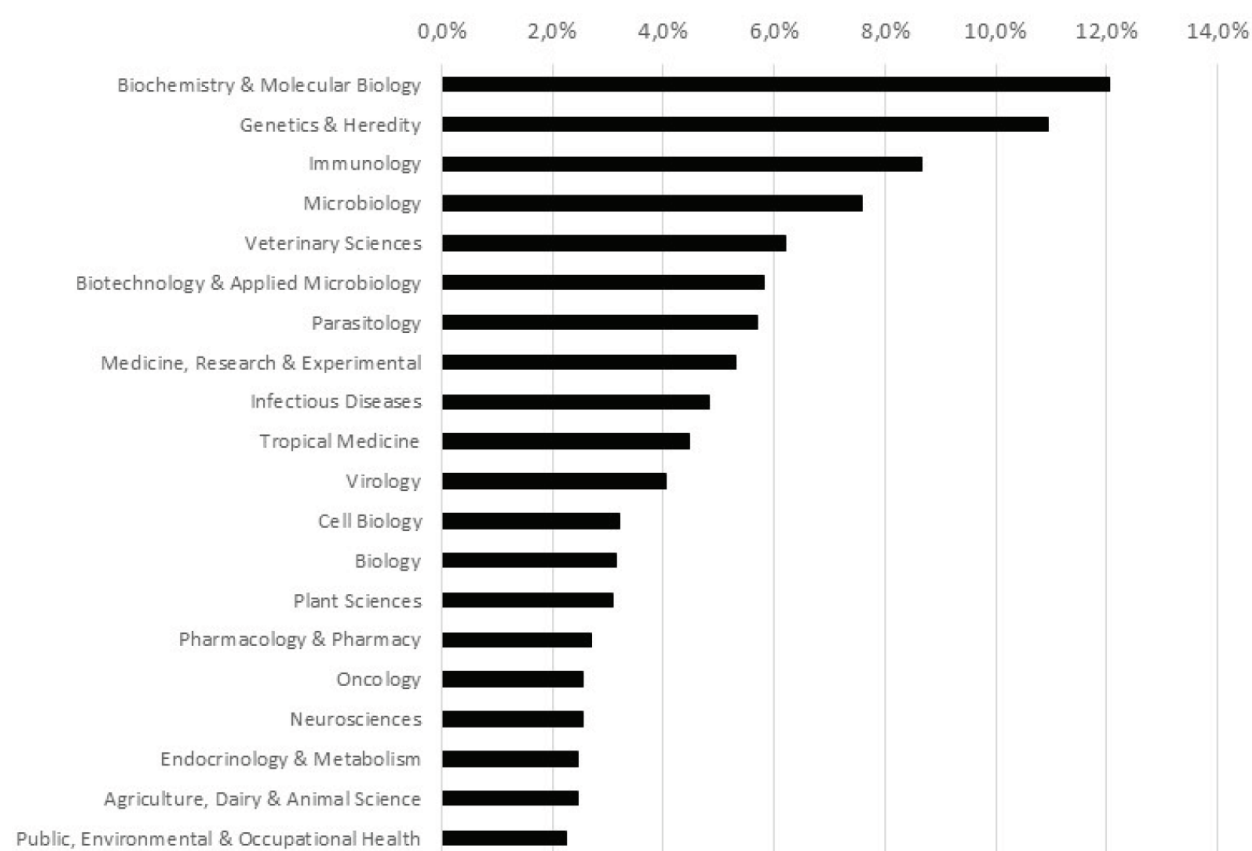

Figure 3. Percentage distribution of scientific publications on biotechnology by areas of knowledge indexed on database. Period 1995–2015.

It can be observed that most of the articles found are in the areas like life sciences and health, highlighting specific areas such as molecular biology, genetics, immunology, and microbiology. The predominance of these areas was already expected due to the characteristics of biotechnology, but it is interesting to note that areas such as molecular biology and genetics have a significant interest toward other traditional areas such as chemical and pharmaceutical industries.

Note, also, that a considerable number of articles are classified as multidisciplinary, confirming that research in biotechnology, as mentioned previously, brings together researchers from different areas of knowledge. This, probably, highlights the increasingly important role of biotechnological techniques for the development of new products.

Of the 73,125 articles published in internationally indexed journals it was possible to realize a trend of publication in two main areas: health and life science. It is worth mentioning that both thematic areas coincide with the prevailing keywords previously identified. Besides this fact, an interesting aspect observes the concerns of the regional coverage of the top 20 journals, which means that the majority of Brazilians scientific articles are submitted in Brazilian journals (60%), or particularly in indexed American journals (30%). This indicator illustrates the little dynamics of international cooperation of Brazilian research groups. Among the indexed journals, the Vaccine journal has the highest number of articles (12.65%), followed by other journals such as Memórias Instituto Oswaldo Cruz (10.98%), and genetics and molecular biology (10.58%).

Figure 4 presents the top 20 journals with a number of scientific publications greater than 40 articles. The list of journals is in accordance with classification presented in **Figure 3**.

An interesting fact observed is the leadership position of Vaccine Journal, which justly gives priority, an analysis of information and knowledge about human vaccines (infectious diseases and noninfectious diseases) and veterinary vaccines, molecular biology, immunology, production and manufacturing, regulatory, and legislation aspects. It is followed by others publications in areas such as microbiology, biology, genetics, life sciences, and others.

Considering the authors´ affiliation, it is observed that there are 441 institutions, showing a high dispersion among the authors´ institutions in Brazil. It is important to highlight the significant number of articles produced by institutions such as the University of São Paulo (USP) representing 32.71%, followed by the Oswaldo Cruz Foundation (FIOCRUZ) with 8.92%, and the Federal University of Rio Grande do Sul (UFRGS) with 7.58% articles, respectively. Another significant topic to be observed is the prevalence of public governmental institutions such as research centers or universities, evidencing a concentration of activities in biotechnology by public institutions or nonprofits corporations at research levels. It is also worth mentioning a few numbers of scientific publications indexed by the Brazilian biotechnology companies in the research period, less than 1%, which indicates a small number of companies working in that area or that they are still consolidating their capacities, according Santana et al. [2]. It is should be highlighted the public institution Brazilian Agricultural Research Corporation (EMBRAPA) Genetic Resources with the 8th institution in the ranking, which is the public company with
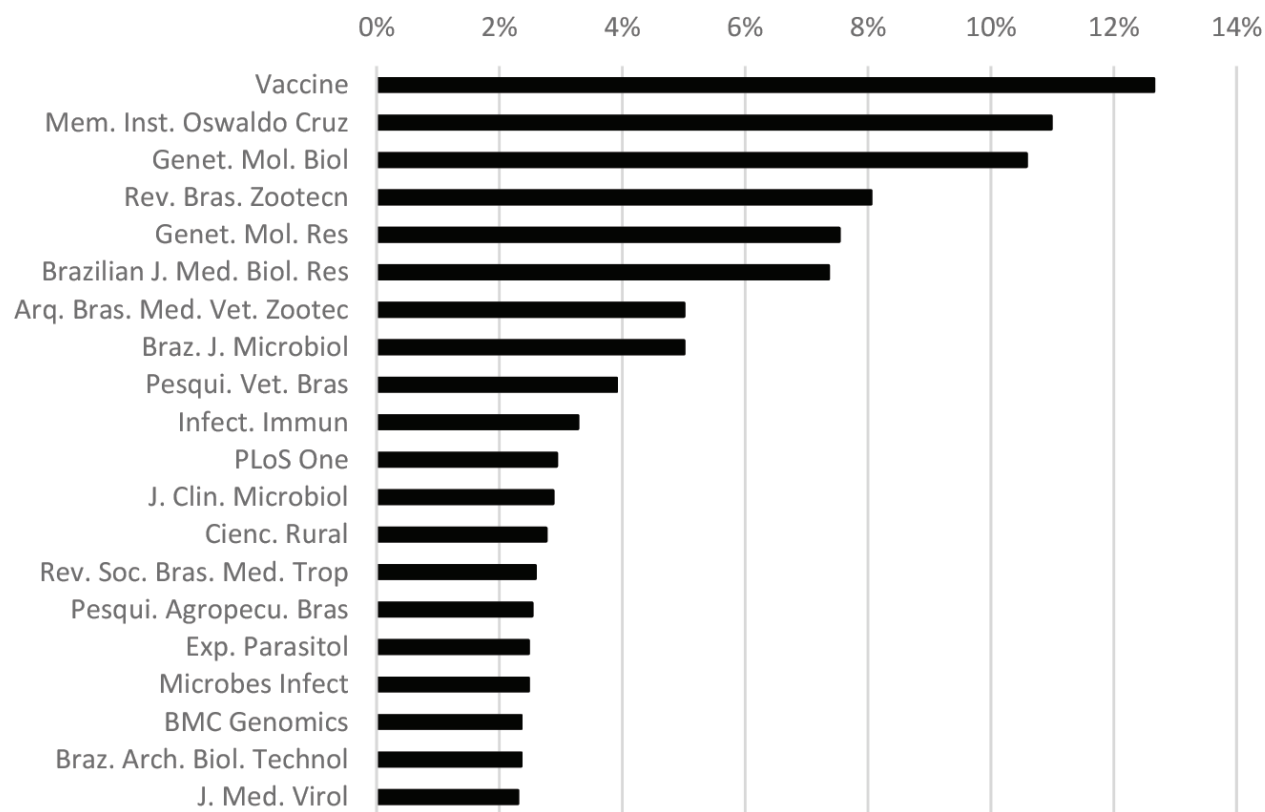
Figure 4. Main internationally indexed journals with biotechnology-related articles.

leadership in transgenic research in the agricultural area in the country. **Figure 5** shows the top 20 institutions that have published more than 100 articles in the observed period.

The research results present that the most of institutions are located in South/Southeast regions, which are more developed regions of the country. There is little representation of institutions in the Center-West/ Northwest regions, presented only for 4 universities: University of Brasília, Federal University of Pernambuco, University of Goiás and Federal University of Ceará.

In addition, there is the significant presence of the public universities of São Paulo (USP, UNESP, and UNICAMP), which together account for a significant share of national scientific output in the biotechnology area, that is, 46.31% of published articles in journals are from USP. This observed result was expected because since the beginning of projects development in the biotechnology area (*X. fastidiosa* genome and HGP/Brazil), there was an intensive participation of research groups of these universities. Furthermore, we can mention the continuous financial support from FAPESP foundation for the development of projects in the areas such biotechnology and bioprospection.

4.3. Maps of knowledge and network collaboration

According to Santana et al. [2], regarding the analysis of relationships between composing agents of the National Organizational System of S,T&I, many authors refer to the central idea
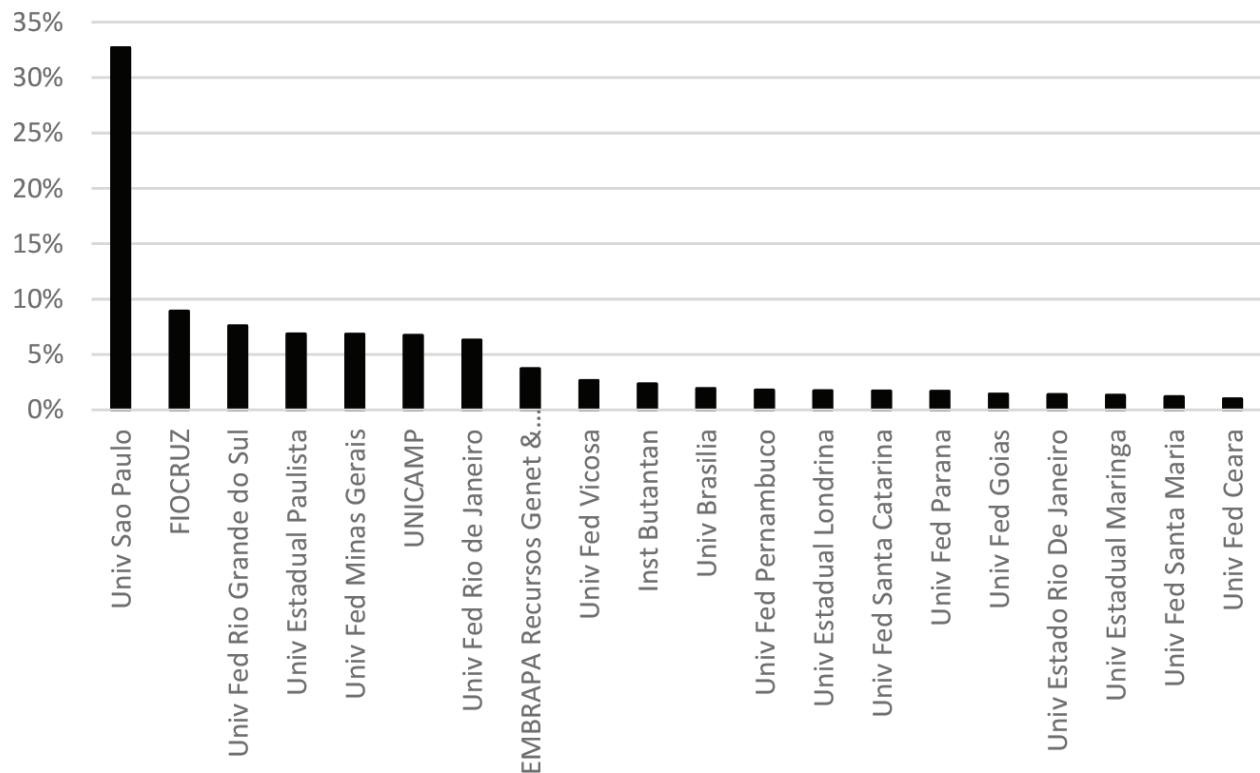
Figure 5. Leading Brazilian institutions with major publications in biotechnology for the period 1995–2015.

of networking and the valuable interactions between system components and its main actors in order to promote the dissemination and use of new scientific knowledge [29].

In accordance with these premises, we sought to analyze the links established between the organizations by observing how these actors relate to each other using the number of publications of scientific cooperation between institutions and countries; on a macro level, the international relationships developed by these institutions for R&D. The best representation of these collaborations is the visualization of maps of knowledge, where the existence or not of correlations and the degree of its intensity are clear, which provide to decision-makers some strategic subsidies in future planning of national activities of ST&I [2].

Considering the network map of articles´ authorship in Brazil, for the biotechnology area, it is possible to verify an intensive cooperation between diverse institutions, especially among Brazilian institutions, showing that 66.9% of articles are written with internal collaboration, which subsidize the relevance to develop endogenous capacity of Brazilian groups and publish papers with little support from international cooperation [2].

It is possible to note groups with strong collaboration such as the University of São Paulo (USP), Federal University of Rio de Janeiro (UFRJ), the University of Campinas (UNICAMP), and Oswaldo Cruz Foundation (FIOCRUZ). These collaborations between Brazilian institutions demonstrate that relationship is based more heavily on the model of interaction between universities, research centers, and nongovernmental research
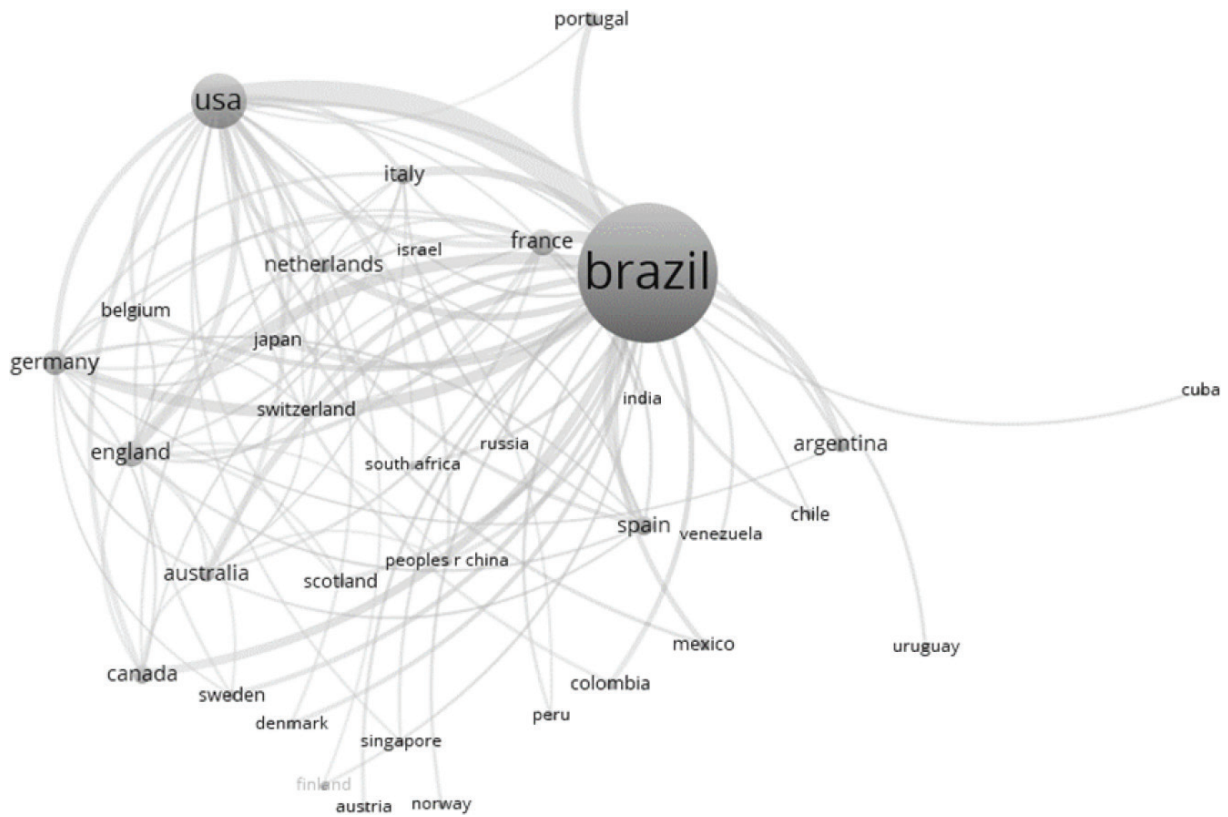
centers and of little interaction with companies. It should be emphasized that this scenario will modify since the implementation of the Organic Law of Science, Technology and Innovation in January 2016, where the private sector was encouraged to invest more in partnerships with public institutions and/or in internal activities of ST&I, aiming to promote alliances between the private sector with scientific research center and universities [2, 29]. **Figure 6** shows the collaboration network among institutions with more than 60 articles published.

From a macro perspective, there is a large international collaboration, particularly with five countries: the United States (12.81%), the United Kingdom (2.27%), France (2.22%), Germany (1.43%), and Spain (1.30%). As seen previously, when focusing on Latin America, the block represents only 1.89% of all countries' collaboration, it is possible to identify that Brazil has networks of scientific collaboration and research with almost all countries. Inside this block, Argentina is a major coauthored number of articles (41.94%), followed by Colombia (19.47%), Chile (12.17%), Uruguay (9.92%), and Venezuela (8.80%). **Figure 7** shows the map collaboration network among 40 major countries and Brazil in the biotechnology area.

Figure 6. Map of institutional relations on biotechnology for Brazil. *Source*: Map presentation software VOSviewer®.

Figure 7. Map of network based on a co-authorship between Brazil and the 40 major countries on the biotechnology area.
Source: Map presentation software VOSviewer®.

5. Conclusions

Traditionally, biotechnology is a technology that is strongly dependent on the studies of the basic research area. Its great success in any country is strongly related to government policies regarding the incentive of science and its technological diffusion. This chapter presents the growing of scientific research on biotechnology in Brazil, over the number of scientific articles published in the area, showing a higher growth of 1.930%, in the last 20 years, more specifically in the last 5 years. With respect to searched terms, "Vaccine," "PCR," and "DNA" are among the terms most frequently applied, being cited, since 1995, by the authors as keywords in scientific journals as well as in relevant journals such as Vaccine and Mem Inst Oswaldo Cruz. Terms such as proteomics and stem cells, related to the frontier area of knowledge, have also appeared in this scientific research. This fact indicates that the research in this area in Brazil is consistent with worldwide trends. Another significant topic is that the biotechnology research in Brazil is very important for studying the country's social problems, especially related to tropical diseases, which presents itself as an important starting point for formulating policies on ST&I, since decision-makers should encourage links between scientific institutions and companies. It is important to point out that Brazilian agricultural biotechnology research has taken significant steps toward the development and use of innovations for sustainable production systems that provide safer food (biofortified foods with vitamins, minerals, and better quality proteins).

A wide dispersion in relation to the thematic areas of biotechnology is observed, however, concentrated mainly in areas such as biochemistry and molecular biology and genetics and heredity. Three institutions are highlighted here: São Paulo University (USP), Oswaldo Cruz Foundation (FIOCRUZ), and Federal University of Rio Grande do Sul (UFRGS). It is worth mentioning that institutions that carry out scientific research in this area are primarily governmental. Regarding the analysis of relationships between agents that compose the National System of Science, Technology and Innovation in Brazil, it was found that for biotechnology, there is a large network of cooperation among international and national institutions, as well as networking among many countries that present a positive factor in the biotechnological development of a country [2]. In conclusion, it was possible to identify the United States as a major coauthor of scientific publications relating the subject, but there are also partnerships with other Latin American countries such as Colombia and Argentina.

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