

Translational research and innovation systems in health: implications on the biopharmaceutical segment

Pesquisa translacional e sistemas de inovação na saúde: implicações para o segmento biofarmacêutico

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ABSTRACT The analysis of the dynamics of innovation in health in the context of the National System of Innovation in Health reveals the potential of the articulation of Science, Technology and Innovation (ST&I) institutions with the Health Economic-Industrial Complex (HEIC), in view of the interactions between universities and research institutes with the productive sector. Translational health research depends heavily on the dynamics and relative situation of the HEIC in Brazil regarding the international context. The study analyzes the interactions between pharmaceutical companies and health research groups in the country, using microdata from the CNPq Research Group Directory database (DGP-CNPq), in a methodological approach appropriate to collaborative network studies. Furthermore, it shows the presence of a network of interactions with the productive sector in the biopharmaceutical area and highlights the potential of several Brazilian ST&I institutions to foster the development of the health innovation system. This interaction may acquire a translational perspective for the use of technological knowledge by the Brazilian society insofar as it is articulated with the development of the HEIC in Brazil as a critical link to meet the demands of the Unified Health System.

KEYWORDS National Science, Technology and Innovation Policy. Health Sciences, Technology, and Innovation Management. Translational medical research.

RESUMO A análise desenvolvida sobre a dinâmica de inovação em saúde no contexto do Sistema Nacional de Inovação em Saúde revela as potencialidades da articulação das instituições de Ciência, Tecnologia e Inovação (CT&I) com o Complexo Econômico-Industrial da Saúde (Ceis), a partir da interação entre as universidades e os institutos de pesquisa com o setor produtivo. A translação em saúde depende fortemente da dinâmica e da situação relativa do Ceis no Brasil ante o contexto internacional. O estudo faz uma análise das interações entre empresas farmacêuticas e grupos de pesquisa em saúde no País dos microdados da base de dados do Diretório de Grupos de Pesquisa do Conselho Nacional de Desenvolvimento Científico e Tecnológico (DGP-CNPq), utilizando uma abordagem metodológica apropriada aos estudos de redes de colaboração. Ademais, mostra o potencial de diversas instituições de CT&I brasileiras, revelando a presença de uma rede de interações com o setor produtivo na área biofarmacêutica, com potencial para o desenvolvimento do sistema de inovação em saúde. Essa interação poderá adquirir, de

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fato, uma perspectiva translacional para a utilização do conhecimento tecnológico pela sociedade brasileira na medida em que seja articulada com o desenvolvimento do Ceis no Brasil, como elo crítico no qual a pesquisa se transforma em produção de bens e serviços para atender às demandas do Sistema Único de Saúde.

PALAVRAS-CHAVE *Política Nacional de Ciência, Tecnologia e Inovação. Gestão de Ciência, Tecnologia e Inovação em Saúde. Pesquisa médica translacional.*

Introduction

The study of innovation in health presents at least two aspects that permit to place it at a special field of analysis. The first one regards the interactions between the system of innovation in health and the systems of social welfare, and the unfolding that results from this interaction in terms of the relationship between health and socioeconomic development. The second aspect regards the complex character assumed by innovation in health, involving close interaction between the segments of industry and services delivery, which acquires an integrative and systemic dimension of the activities performed within the Health Economic-Industrial Complex (HEIC), considered as an interdependent productive space of research on health and development of related activities.

Health connects several segments of knowledge-based industries, at the same time that it is a highly strategic area of society and occupies a privileged locus in public policies and national political debate. As stressed by Gadelha et al.¹, the great challenge to the economic analysis in health is the need to articulate a systemic vision of the health area that simultaneously encompasses the economic logic and the sociosanitary logic, capturing the tensions and interfaces that exist between them.

Health innovation presents an important interaction with the process of basic research, which is fostered by the scientific sector. On the one hand, knowledge produced by the

scientific and technological infrastructure in the health area fosters an innovation flow that tends to shape the operation of health services and medical practices from the use of new medicaments, medical equipment, or clinical procedures; on the other hand, medical practice has a central role in health innovation, insofar as it constitutes the origin of important information flow that establishes new agendas for scientific research.

Therefore, one of the main challenges to the analysis of innovation in health lies in the construction of analytical models that, besides taking into account the systemic and integrative character of innovation in the health service sector, also encompass the inherent complexity of articulation and interaction established between the different segments of actors taking part in the National System of Innovation in Health, which reflect on the production and innovation dynamic of HEIC^{2,3}.

It can be stated that, when considering political-economic-institutional realities, translational research depends on the existence of a productive base in health that constitutes the decisive link for translation to occur, hence creating economic and social wealth. It is this feature, at once systemic and structural, that permeates this paper, since it places the biopharmaceutical segment in the context of the health productive system (HEIC) as an analytical and political challenge, considering the centrality of biotechnology in health, both

for innovation and for its absorption in the productive base, and in the generation of benefits to the Brazilian society.

The concept of translational research emerged in the context of research efforts conducted at the National Cancer Institute (NCI) of the United States of America, in the early 1990s, with the purpose of promoting interdisciplinarity, connecting and accelerating the bidirectional exchange between basic science and clinic throughout the various stages of Research, Development and Innovation (RD&I) in the health field. Gradually, the concept of translational research incorporated increasingly broader aspects of innovation cycles in different health segments, from scientific research and technological development to the final links related to clinical trials, regulation and commercialization⁴. This perspective constitutes a substantial advance when analytically understood as a development towards a vision in which the analysis of the innovation process in the context of health assumes a systemic character. The translational research approach requires its conceptual incorporation in the analysis of national innovation systems, with emphasis on its systemic character and national dimension, which are essential regarding the political and institutional organization of the local context, actors, and interactions for the generation and diffusion of innovation, in a still markedly asymmetrical political and economic reality⁵.

Based on this general referential frame, this paper aims to present an exploratory analysis on the articulation between the infrastructure in Science, Technology and Innovation (ST&I) and the health productive base, by means of an evaluation of the efforts on knowledge transfer between the scientific sphere and the private sector. The analysis focuses on the interactions between research groups in the areas of biological and health sciences, registered on the Directory of Research Groups of the National Council for Scientific and Technological Development (DGP-CNPq), and other components of the Brazilian biopharmaceutical

innovation system, among which there are national and multinational pharmaceutical companies, micro and small biotechnology-based firms, and public pharmaceutical laboratories.

Material and methods

The elaboration of this paper is grounded on different databases and secondary sources of information regarding the conceptual, analytical and methodological discussions involving the relationship between scientific research and innovation in the health field. In a methodological approach to capture the dynamic of the biopharmaceutical segment, the analysis focused on the interactions between pharmaceutical firms and health research groups in the country. The study used CNPq database, with data made available by the DGP censuses according to the microdata on interaction of the 2016 Census of DGP-CNPq, referring to the period 2014-2016. The study of the evolution of relationships through time is not possible because the interaction microdata for the other censuses are not available, although indicators aggregated by areas of knowledge are available for the period 2002-2010 on the tabular plan of CNPq directory (2018). Data analysis was conducted by means of crossing between DGP-CNPq microdata and a sample of 385 firms through the comparison of the Corporate Taxpayer National Register (CNPJ, in Brazil) of partner institutions involved in university-firms interactions. Data of CNPq directory permit the distinction between different areas of health knowledge – involving disciplines of both strictly medical and biological sciences fields – enabling the discussion of the evolution of scientific competence distribution through the country's regions and the relationships established by research groups with firms and other institutions. With the purpose of covering all the health-related fields of competence, 23 fields of knowledge linked to the 'broad areas' of Biological Sciences and Health Sciences were

included. On the DGP-CNPq questionnaire there are 14 types of relationships that can be chosen by the leader to characterize the relationship with firms⁶.

Interactions between elements comprising the productive base of pharmaceutical and biopharmaceutical industries in Brazil and the national science and technology structure permits the analysis of collaboration networks based on graph theory. A graph is a diagrammatic representation of an interconnected structure consisting of a set of elements named nodes (vertices) that are interconnected in pairs by one or more types of interdependence (edges, links or connections). A network is a set of graphs from which it is possible to analyze the process of grouping and configuration of the nodes⁷.

This paper is structured in three sections, besides the introduction. The second section presents the methodological aspects of the analysis developed drawing on DGP-CNPq database. The third section presents the main results of the analysis, drawing on the conceptual and analytical synthesis on the concept of health innovation systems and its relation with the elements that form the referential frame of translational research. Furthermore, the section presents the outcomes of the survey on the interactions between Science and Technology Institutions and the other actors that are part of the national biopharmaceutical productive base according to CNPq database. The fourth section presents the main conclusions of this study.

Results and discussions

This section is structured around two axes of analysis. The first one has a conceptual and analytical character and seeks to highlight the importance of the systemic dimension of health innovation on the space where the actual realization of health production occurs (in the ambit of HEIC), considering the increasing complexity of the cycles of

technological development of products in this field, especially in the case of pharmaceuticals and medication. The second axis explores the present pattern of interactions between the scientific and technological infrastructure and firms of the biopharmaceutical segment in Brazil.

Health innovation systems

The disaggregation of the concept of Innovation System drawing on its sectorial, territorial or technological components constitutes a widely followed pathway in the ambit of the neo-Schumpeterian³ approach. Gelijns and Rosemberg⁷, from a review of studies on the interactions between industry, university, and medical care systems, draw on a systemic conception to analyze the complexity associated with the information flows and the mechanisms of generation, diffusion, and use of innovation in the health field. As pointed by the authors, the delivery of new medical technologies involves, firstly, knowledge bases that are increasingly interdisciplinary and impose the interaction between individual actors of different disciplinary backgrounds. In the pharmaceutical field, for instance, the development of a new medication requires the cooperation between professionals from backgrounds on organic chemistry, molecular biology, immunology, toxicology, chemical engineering, medicine, among others. This diversity is also evident in the innovation process of medical equipment, involving the incorporation of scientific knowledge and technological advances from external fields (physics, engineering, microelectronics, materials, optics, etc.) for the incorporation in medical applications. The innovation process involves a strong interaction and the construction of effective communication channels between physicians and health professionals with physicists and engineers. Secondly, besides the inter and multidisciplinary character, innovations in the health field are strongly based on forms of interinstitutional interaction, especially between universities and research institutes with industries.

In the specific context of the approaches on health industries, it is worth noticing the concept of medical-industrial complex proposed by Cordeiro⁸, emphasizing the various forms of articulation involving activities of medical assistance, professional education networks, and segments of the pharmaceutical industry and medical equipment. However, this approach stresses only the space of capital circulation, revealing a tension with the social needs, not considering the ambit of wealth and, even, innovation generation. The approach of HEIC, published for the first time in 2003², seeks to integrate the ambit of circulation with the ambit of production and innovation and the role of the State in the promotion and regulation of the health productive system, as recently highlighted in Gadelha and Temporão⁹, who revisit this theoretical pathway of constitution of a research program, including its application in public policies.

In a broad perspective, innovations in the health field involve not only the introduction of new medicaments and equipment but also the adoption of new medical practices in health services delivery. This process occurs from the articulation of a broad set of actors and institutions responsible for the creation, dissemination and use of innovation along various phases with a high degree of interdependence. In this context, besides the development of tangible products such as medicaments and equipment, there is a strong intangible component in health innovation that is associated with clinical practices, institutional arrangements, treatment protocols, and other types of medical artifacts, that permit differentiate at least three distinct innovations in the health field¹⁰:

- Biomedical and biopharmaceutical innovations associated to the discovery of new medicaments, molecules and compounds;
- Tangible medical innovations associated to new equipment and technological systems of diagnosis and therapy;

- Intangible medical innovations such as new protocols, medical practices and management of medical services delivery.

Among the contributions that seek to understand the specificities of the health innovation system in Brazil, there are those of authors Albuquerque and Cassiolato¹¹ and Gadelha², besides others. In the approach of HEIC, which emphasizes the space of competitiveness and reproduction of capital in health, an effort can be observed to update this systemic and structural perspective to the contemporary context drawing on authors as Gadelha, Vargas, Maldonado et al.³; Costa et al.¹², and Gadelha and Temporão⁹, among others.

Among the general characteristics of the systems of innovation in health, it can be highlighted that:

- a) Universities and research institutions play a central role in the flow of information and scientific and technological knowledge established with the other components of the National System of Innovation in Health, especially with the industry and the public health system, considering the intensive character of knowledge inherent to the innovation process in the health area;
- b) The subsystem of services plays a fundamental role both in the implementation and diffusion of innovation in the health area and in the qualification of demands for the other subsystems of chemical and biotechnological base and equipment. Health services delivered at hospitals, clinics and primary care clinics have an important participation in knowledge flows involving both the industry and universities and research institutes;
- c) The institutional and regulatory frameworks represent an important instance of selection of innovations generated in the industry and constitute a significant particularity of the health sector insofar as

they represent a non-mercantile selection environment;

d) The productive base presents various degrees of interaction with the scientific and technological infrastructure, marked by the convergency of different pathways and technological platforms related to biotechnology, nanotechnology, and Information and Communication Technologies (ICT);

e) The Health System, conditioned by the specificities of the assistential model, plays a mediation role between HEIC and ST&I infrastructure in the delivery of health demands. Innovations that are implemented in the ambit of the Brazilian Unified Health System (SUS) are directly reflected on social wellbeing indicators.

In the Brazilian case, it is also observed an additional set of systemic and structural factors that condition the productive and innovative dynamic of the health sector, among which stand out:

a. Existence of specific epidemiological profiles with the prevalence of both infectious diseases, neglected by the global science and industry, and non-transmissible chronic diseases, that become predominant in the disease burden together with external causes (traffic accidents and violence);

b. Fragility of the health productive base that presents strong dependence on imported input materials, reduced entrepreneurship scale, and low rate of innovation at the pharmaceutical and equipment industries. Such hindrances have enlarged the National Health System vulnerability and the deficit of HEIC trade balance;

c. Existence of important 'windows of opportunity' associated with the new technological platforms of biotechnology, nanotechnology, and microelectronics permitting new

applications in the field of prevention, diagnosis and therapy;

d. The existence of national scientific capacitation in the biomedical and biotechnological areas and the significant increase of scientific production in the health area do not reflect on the technological performance and reveal hindrances in the interaction between the scientific infrastructure and the productive base.

Science & Technology Institutions and university-firm interaction networks in the biopharmaceutical segment

The present configuration of the production and innovation system of the biopharmaceutical segment in Brazil (one of HEIC subsystems) involves the articulation of different sets of institutional actors and enterprises segments among which can be highlighted: i) universities and research centers; ii) public institutions of research and production of medicaments and immunobiologicals; iii) micro, small and medium enterprises of biotechnology and biosciences in human health involved in specific niches of the RD&I chain of chemical and biotechnological base; iv) national and multinational pharmaceutical enterprises installed in the country.

Universities and research centers constitute a fundamental link of the innovation system of the chemical and biotechnological based industry. Despite not being directly involved with pharmaceutical products and services, they have a central role in activities of research and human resources capacitation. Besides providing professional education, universities are convergency centers of information flows that originate in their own researches and from interactions with enterprises, regulatory agencies, hospitals, clinics, primary care clinics, among other actors capable of transmitting new demands to the pharmaceutical industry^{13,14}.

A second element that is part of the Brazilian biopharmaceutical innovation system is represented by technology-based enterprises directed to research, development and delivery of specialized life-sciences knowledge-intensive services and the utilization of biotechnology techniques. During the last decade, several studies have sought to improve the mapping of this universe of enterprises. These studies point to the existence in Brazil of approximately 300 biosciences enterprises and between 175 and 240 biotechnology enterprises constituted as micro, small, and medium technology-based firms. These enterprises are for the most part: young; micro and small; concentrated in the Southeast region, especially in the states of São Paulo and Minas Gerais; specialized in the delivery of biotechnological services or as products and processes developers; in pre-operational phase and largely controlled by national capital. Alves¹⁵ provides a methodology for the prospection of enterprises that enabled the identification of Brazilian firms as follows: 271 of biosciences, 137 of biosciences with application in human health, and 96 of biotechnology in human health.

Public institutions of research and production of pharmaceuticals and immunobiologicals, on their turn, constitute an important peculiarity of the health productive base in Brazil. Despite being quite a heterogeneous segment, their origin is mostly associated to supplying the demands of the policy of pharmaceutical assistance and national production of vaccines and essential medicaments. These institutions supply 80% of the domestic demand for vaccines and presently they lead the national efforts of the biopharmaceutical production^{1,2}.

As one of the central links of the pharmaceutical productive base there are the segments of national and multinational pharmaceutical laboratories. The large multinational pharmaceutical corporates, which dominate the global market,

in 2010 controlled approximately 50% of the Brazilian pharmaceutical market, whereas in 2015, according to data from Sindusfarma/IMS Health, this participation was of 43%. Despite bringing to Brazil the stages of production and distribution, multinationals maintain their innovation efforts concentrated at their matrices abroad. In the case of national pharmaceutical laboratories, although the standard of Research and Development (R&D) investment in the segment is quite distant from that of the global pharmaceutical industry, it is verified that in recent years there has been a significant increase in the rates of innovation and changes in the investment structure of R&D. The structural alterations on the standard of innovation of national pharmaceutical enterprises can be attributed to a virtuous cycle of development in this sector in the country, which is the result of a significant convergency of the industrial and innovation policy and the health policy¹⁶.

Although in Brazil there is a wide range of institutions with consolidated research groups on biological and health sciences, it is observed that one of the main challenges for the insertion of the country in the new strategic technological platforms in the health area (biotechnology, nanotechnology, and ICT) is related to the existing discrepancy between the level of scientific capacitation and the limited capacity for innovation within HEIC^{13,14,16}.

A critical issue for the development of the biopharmaceutical segment is the existence of hindrances in the process of transfer of scientific knowledge produced at the academy to the productive sector. The importance of scientific and technological knowledge overflow can be summarized in three essential arguments^{17,18}: i) knowledge overflow is necessary to enable the development of products and services in compliance with the Brazilian regulatory and phytosanitary requirements; ii) the strengthening of cooperative relationships within the

innovation system is crucial to increase the integration of sectorial agents to the structure of HEIC and promote the construction of capacitation in strategic areas; iii) the construction of competences and capacities in biological and health sciences can be the moving force of the innovation process in pharmaceuticals and biopharmaceuticals, as long as bridges are built between knowledge produced at the academy and the capacitation of the productive sector in development, production, and distribution.

From interactions between research groups registered at DGP-CNPq according to the 2016 Census, and the main identified components of the Brazilian biopharmaceutical innovation system, one observes the existence of a set of 56 Institutions of Science and Technology, which participated in a total of 201 interactions with actors of the productive base such as private pharmaceutical laboratories, national and multinational, micro and small enterprises of biotechnology and public pharmaceutical laboratories.

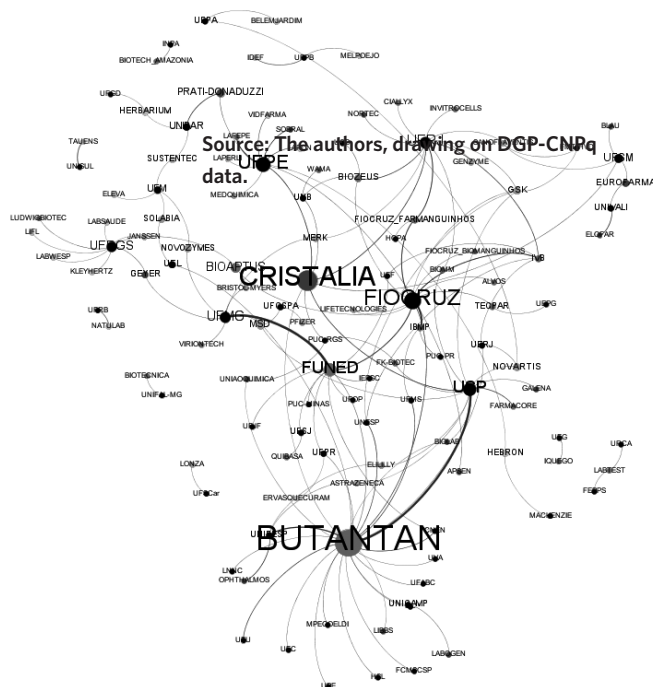
The Institutions of Science and Technology that most interacted with sectorial components were: Oswaldo Cruz Foundation (Fiocruz, 24), University of São Paulo (USP, 21), Federal University of Rio de Janeiro (UFRJ, 17), Federal University of Pernambuco (UFPR, 16) and Federal University of Minas Gerais (UFMG, 15). The most interactive research groups were: Ecology and physiology of microorganisms (UFMG, 4), Industrial Pharmacotechnical Development of Pharmaceutical Products

(UFPE, 6), Galenic Development and Biopharmacy (UFPE, 5), Pharmacology and Pre-clinical Toxicology of Bioactive Products (UFPE, 3), Technology of pharmaceutical products (UFRGS, 5), National Institute of Science and Technology of Pharmaceuticals and Medicaments (INCT-Inofar, UFRJ, 4), Mario Vaisman endocrinology (UFRJ, 3), Development of tests and trials for evaluation of pharmaceutical inputs and products (UFSM, 4), Acute coronary disease (USP, 5), Nucleus of Cell and Molecular Therapy (Nucel, USP, 3).

It is noteworthy that innovation in industries that are strongly knowledge-based is an intrinsically collective phenomenon. Especially in the case of biopharmaceutical activities, interinstitutional and interdisciplinary collaboration is a critical factor to favor the emergence of new products and processes. Partnerships are articulated on knowledge networks that are determinant to competitiveness and the innovation dynamic of pharmaceutical and biopharmaceutical enterprises¹³.

The network of interactions between enterprises, public laboratories, and science and technology (S&T) institutions is presented in *figure 1*. As the study focuses on knowledge networks, the constructed graphs are indirect and finite, so the edges do not have a specific orientation. It is worthy of note that Butantan Institute, Oswaldo Cruz Foundation, and Ezequiel Dias Foundation are at the same time public producers and education and research institutions.

Figure 1. Network of interactions between identified universities, enterprises and institutions



Source: The authors, drawing on DGP-CNPq data.

The network shown in *figure 1* presents 126 nodes and 146 edges. The size of the nodes is presented on the base of a centrality measure – known as intermediation or betweenness centrality – that indicates the importance of the intermediation of each vertex as a point of communication control between all the other nodes on the network. Centrality measures are based on the supposition that information exchanged by means of the multiple interactions tend to follow the shorter paths between the nodes that compose the network.

In this sense, it is possible to state that among the central institutions of pharmaceutical and biopharmaceutical innovation stand out: Butantan Institute, Oswaldo Cruz Foundation (national leader in biological production), Federal University of Pernambuco, University of São Paulo, Ezequiel Dias Foundation, Federal University of Rio de Janeiro,

Federal University of Minas Gerais, and Federal University of Rio Grande do Sul. The strengthening of interactions between research groups of these institutions and productive agents are potentially beneficial to the entire network, which is configured around the efforts of pharmaceutical and biopharmaceutical innovation in Brazil. Also to be highlighted is the centrality of the Brazilian pharmaceutical industry *Cristália*.

The knowledge network composed of multiple interactions between industrial actors, interconnected by research groups and public laboratories, can also be analyzed according to subgroups that compose the productive base, permitting evaluate the differences in terms of interaction patterns between groups of activities. Therefore, the main hubs – vertices that stand out due to their greater potency in terms of relative concentration of connections by nodes – are indicated by groups of activities. For the

group of micro, small and medium enterprises in biosciences, the central institutions are the Federal University of Rio de Janeiro and Oswaldo Cruz Foundation. Considering the national pharmaceutical enterprises, the main hubs are Butantan Institute, University of São Paulo, and Federal University of Pernambuco. For the group of producers of phytotherapies medicaments, the main institutions are Federal University of Pernambuco and Federal University of Rio Grande do Sul. In the segment of public laboratories, stand out Butantan Institute, Ezequiel Dias Foundation, and Oswaldo Cruz Foundation. Finally, for the group of multinational pharmaceutical corporations, stand out the University of São Paulo, Federal University of Rio de Janeiro, Heitor Vieira Dourado Tropical Medicine Foundation, Federal University of Minas Gerais, and Oswaldo Cruz Foundation. The hubs indicate the institutions potentially more conducive of innovation to be supported in each of the identified segments.

Differences among segments can also be evaluated considering the types of interactions between technology and science institutions and their productive partners. Basic research and applied research are the most frequent types of interaction and together they represent 59% of the totality of established interactions. Other frequent types of interactions are technology transfer from group to partner and supply of input material from partner to group. Efforts to effectively transfer knowledge among the scientific and industrial sectors are considered as key-factor to stimulate pharmaceutical and biopharmaceutical RD&I processes.

Regarding scientific research, efforts to jointly conduct basic research are important to expand the knowledge base and promote the development of the absorption capacity of industrial partners, hence propitiating the increase of the innovative dynamic. Efforts involving research with no immediate application of outcomes are more frequent

in the segments of public laboratories and multinational pharmaceutical corporations. On the other hand, efforts put on scientific research that aim at immediate application of outcomes are fundamental to stimulate the development of innovative processes and products. And efforts on joint applied research are more frequently carried out at national pharmaceutical enterprises, producers of phytotherapies, and public laboratories.

Interactions directed at technology transfer among research groups and industrial partners are another important form of promoting overflow of knowledge that is potentially conducive of innovation processes. However, in order to have efficient technology transfer it is necessary to create stable and bilateral communication channels (technology transfer from group to partner and from partner to group). Data analyzed indicate that in the case of Brazil, transfer of knowledge is more intensive in the flows of knowledge originating in research groups and transferred to industrial partners. There are evidences of bilateral technological transfer between: pharmaceutical enterprise Cristália and Federal University of Rio de Janeiro; biosciences enterprise Farmacore and University of São Paulo; Butantan Institute and National Laboratory of Scientific Computing; and Butantan Institute and University of São Paulo.

Institutions and research groups with larger proportions of interactions are presented on *chart 1*. The University of São Paulo and the Federal University of Minas Gerais stand out for their efforts regarding R&D, whereas the Federal University of Pernambuco stand out for efforts regarding innovation. The Federal University of Rio de Janeiro and the University of São Paulo present evidences of their relevant performance in services delivery. Oswaldo Cruz Foundation stands out in all three types of efforts. It is worthy of note that Butantan Institute and Ezequiel Dias Foundation do not appear on *chart 1* because their captured interactions are related to the performance

of productive activities with industrial partners. *Chart 1* is one among possible indicators to highlight the relevance of Science and Technology Institutions; it is necessary to

consider other factors such as the participation at knowledge networks, on national and international ambit, as shown on the chart.

Chart 1. Main institutions and research groups by type of interaction efforts with productive actors

Institutions	Research Groups
Oswaldo Cruz Foundation (Fiocruz)	Molecular Biology and Endemic Diseases, Proteins e Peptides Biochemistry, Democratization of Scientific and Technical Information on Health, Development of reagents, input materials and equipment for Diagnosis, Diagnosis and molecular epidemiology of bacterial meningitis, Genomics and Computational Biology, Functional Genomics, Hantavirus and Rickettsia infections, Immunology of Invertebrates, Innovation for Diseases of Neglected Populations (IDPN), Laboratory of Biology and Parasitology of Reservoir Sylvestral Mammals, Laboratory of Experimental Schistosomiasis (LEE), Laboratory of Inflammation and Biomarkers (LIB), Laboratory of Cardiovascular Investigation, Laboratory of Genic Expression Regulation, Laboratory of Virologic Technology, Neurogenomics, New therapeutic approaches based on technological innovation, Nucleus of Technological Development of Pharmaceuticals of Natural Origin (NDTec-Far), Clinical Research and Public Policies on Infectious and Parasitic Diseases, Research and quality control of bioactive substances, Proteomics and Protein Engineering, Taxonomy of phlebotominae/Epidemiology, diagnosis and control of leishmaniasis.
University of São Paulo (USP)	Redox Processes in Biomedicine Redoxoma (Cepid), Acute Coronary Disease, Genetics of microorganisms and biotechnology, Genetics and molecular hematology, Group of Cell Adhesion and Movement, Institute of Investigation on Immunology, Immunopathology of Infectious Diseases, Inflammation and sepsis, Laboratory of Immunology of the Institute of Heart (InCor-HCFMUSP), Laboratory of Basic Research on Nephrology (LIM 12), Nucleus of Cellular and Molecular Therapy (Nucel), Nucleus of Research on Vaccines, Biopharmaceuticals and Immunomodulators, Research, Development and evaluation of cosmetic products, Regulation of phagocyte function.
Federal University of Minas Gerais (UFMG)	Advances on hematologic research: hemostatic, cellular, biochemical and molecular aspects, Biodiversity and bioprospection of fungi, Molecular biology and immunology of gynecological cancer, Center of Technology for the Development of Medicaments CT - Pharmaceutical Technology, DPLF - Nucleus of Development of Polymeric Devices for Drug Release, Ecology and physiology of microorganisms, Biochemical and Molecular Pharmacology, Group of Investigation of Uveitis/Ocular Inflammatory Diseases, Group of Research of on Mycobacteriosis, Laboratory of Viruses UFMG (LABVIR), Nucleus of Research on Clinic and Laboratorial Hematology, Brazilian Group of Congenital Toxoplasmosis.
Federal University of Pernambuco (UFPE)	Biotechnology of Bioactive Natural Product, Industrial Pharmacotechnical Development of Pharmaceutical Products, Galenic Development and Biopharmacy, Pharmacology and Pre-clinical Toxicology of Bioactive Products, Applied Microbiology to obtain bioactive products.
Federal University of Rio de Janeiro (UFRJ)	Pharmaceutical Biotechnology, Pharmacology of Muscle Excitation-Contraction, Biological Physics, Research Group on Antileishmanial Nanopharmaceuticals and Vaccines, National Institute of Science and Technology of Pharmaceuticals and Medicaments (INCT-INOFAR), Laboratory of Pharmacology of Pain and Inflammation, Laboratory of Hemostasis and Poison - Unity of Mass Spectrometry and Proteomics, Mário Vaisman endocrinology, Nanoradiopharmaceuticals & new radiopharmaceuticals, Nucleus of Research and Identification of Natural Antimicrobials, Study Network of Natural Products for Antimalarial Therapy, Enzymatic Technology.

Source: The authors, drawing on DGP-CNPq data.

An alternative manner to evaluate the relevance of Science and Technology Institutions to the dynamism of knowledge-based activities in biological sciences and health is to consider

the relative potency of the participation of these institutions at more complex knowledge networks, which actually are information convergence centers in a systemic environment,

Oxford, University of Cambridge, Harvard Medical School and Public Health School, Johns Hopkins School of Public Health, Institut Pasteur, among other important motors of scientific and technological advance of the World System of Pharmaceutical and Biopharmaceutical Innovation. In the same way, the Brazilian Science and Technology Institutions that are most capable of connecting the pharmaceutical and biopharmaceutical industry with the large networks of global scientific research, considering the global articulations, are: University of São Paulo, Oswaldo Cruz Foundation, Federal University of Rio de Janeiro, Butantan Institute, State University of São Paulo, State University of Campinas, Federal University of Pernambuco, Federal University of Rio Grande do Sul, University of the State of Rio de Janeiro, Federal University of São Paulo, Ezequiel Dias Foundation and Federal University of Minas Gerais.

Final considerations

The analysis presented in this paper, still with an exploratory character, on the dynamic of innovation in health in the context of the National System of Innovation in Health, reveals the articulation potentialities of the ST&I institutions with HEIC, drawing on the interaction of universities and research institutes with the productive sector. Translation in health heavily depends on the dynamic and relative situation of HEIC in Brazil regarding the international context. The existence of a dynamic and productive base in health is presented as the great challenge to have knowledge transformed into innovation and that it can be accessed by the Brazilian society, by means of the incorporation of its production into the services delivered by SUS.

The study shows the potentiality of several Brazilian ST&I institutions, revealing the presence of a network of interactions with the

productive sector in the biopharmaceutical area, thus highlighting the potential of health science in Brazil for the development of the system of innovation in health. This interaction can in fact achieve a translational perspective for the utilization of technological knowledge by the Brazilian society insofar as it is articulated with the development of HEIC. This productive system presents itself as a crucial link, permeated with competitive conflicts and asymmetries on the global scale, to make feasible that the knowledge fostered by research and development generated in Brazil may have its application directed to the needs of health, and specially of SUS, simultaneously creating jobs, income, investment, and innovation in the country.

The translation, articulated to a national strategy of development, should involve the relation of health and ST&I policies with the industrial and productive development policies, in order to consider actual health problems as the starting point and to orient health research, when related to the achievement of new health products and services. At the same time, the systemic articulation of these policies should result in the increase of technological capacitation in the ambit of HEIC, reducing the strong national dependence and vulnerability in health, which structurally limit the universal access and the right to health.

Collaborators

Gadelha CAG (0000-0002-9148-8819)* participated in the coordination of the conception, outline and analysis. Vargas MA (0000-0001-7954-8594)* contributed to the conception, planning, analysis and data interpretation. Alves NG (0000-0002-8178-3793)* contributed to the support to the conception, research and methodology with emphasis on the identification of collaboration networks.* ■

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