Longitudinal Analysis of Patents on Colorectal Cancer

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Abstract

colorectal cancer is epidemiologically relevant worldwide because it is the fourth leading cause of death from cancer. This study aims to present the mapping of technologies related to colorectal cancer. The search took place during the months of May and June 2019. The Leans database was used, which collects global patent information. The search occurred through the term "colorectal cancer", inserted in the title or abstract fields. Patents with publication date between January 1, 2000 and June 1, 2019 were selected. Only the patents granted and those filed were filtered (patent application; granted patent). A total of 6,850 patents were identified, of which 5,445 (79.48%) correspond to patents filed and 1,405 (20.51%) are patents granted in the period from 2000 to 2019. In 2000, 47 patents on colorectal cancer were published. The quantitative growth of technologies filed and granted was constant. In 2017 there was a total of 911 applications, indicating a growth of 1938.29% in relation to the year 2000. The first patent of the period was on the APC gene mutation, associated with colorectal cancer in families of Ashkenazi Jews, developed by Laken and collaborators (2000), and belongs to Johns Hopkins University, Baltimore, Maryland, in the United States. It can be concluded that the mapping of patents is important to trace a panorama of the world technological advance, as well as it can also be used as an instrument to identify scientific articles that cite patents developed in a given time space.

Keywords: patents; colorectal cancer; technological advances.

1. Introduction

Currently, one of the main public health problems worldwide is cancer, which is a chronic degenerative disease that affects several dimensions of human life, causing economic impact on society, because it requires specialized treatment prolonged and costly. It is also considered responsible for reducing the potential of human labor and the loss of many lives, which can have an impact on the financial aspect of

organizations (INCA, 2018).

The National Cancer Institute José Alencar Gomes da Silva (INCA) and the Ministry of Health (MS) estimate the occurrence of about 600 thousand new cases of cancer in Brazil in 2018. The precise number of the estimate is 582,590 new cases of cancer: 282,450 in women and 300,140 in men. The study covers the 2018-2019 biennium and the estimates for 2019 are the same as for 2018. In a projection, more than 15 million new cases of cancer are expected worldwide for the year 2020 (INCA, 2018).

Cancer of the colon and rectum has epidemiological relevance worldwide, since it is the third most commonly diagnosed malignant neoplasm and the fourth leading cause of death from cancer (FERLAY et al., 2013). A large geographical variation has been observed, with high rates in more developed countries compared to those less developed (CENTER; JEMAL; WARD, 2009; FERLAY et al., 2013).

Geographic patterns are very similar between men and women, but rectal cancer is about 20% to 50% higher in men in most populations. The number of new cases of colon and rectum cancer (more commonly called bowel cancer) estimated for Brazil for each year of the 2018-2019 biennium is 36,360 in both sexes, 17,380 new cases in men and 18,980 in women. These values correspond to an estimated risk of 16.83 new cases per 100,000 men and 17.90 per 100,000 women. It is the third most frequent type of cancer in men and the second among women (INCA, 2018).

Colon and rectal cancer in men is the second most frequent in the Southeastern Region (23.29/100,000) and the third in the Southern (22.17/100,000) and Midwestern (16.95/100,000) Regions. In the Northeast (7.98/100,000) and North (4.97/100,000) regions, it occupies the fourth position. For women, it is the second most frequent in the Southeast (23.86/100 thousand) and South (22.92/100 thousand) regions. In the Midwestern (17.98/100,000), Northeastern (9.52/100,000) and Northern (7.38/100,000) regions, it is the third most frequent, not considering non-melanoma skin tumors (INCA, 2018).

Incidence and mortality rates from colon and rectal cancer vary widely around the world according to the Human Development Index (HDI), with three patterns of disease distribution being identified: (1) increase in both rates in recent decades in countries that underwent a rapid economic transition, including Brazil; (2) increase in incidence and decrease in mortality in countries with high HDI, including Canada, United Kingdom, Singapore and Denmark; and (3) decrease in both rates in countries with very high HDI, such as the United States, Japan and France (ARNOLD et al., 2016; GASPARINI et al., 2018). So the research question is: what is the current panorama of technologies related to colorectal cancer? The overall objective is to map patents on colorectal cancer.

2. Theorical Framework

2.1 Colorectal cancer

CRC is a multifactorial disease influenced by genetic, environmental and lifestyle factors (SANDLER, 1996; BOYLE; LEON, 2002; CAMPOS et al. (2017). Hereditary factors, such as family history of CRC and inflammatory bowel diseases, represent only a small proportion of the variation observed in the overall burden of disease. In this sense, the geographical differences observed in incidence possibly reflect the adoption of western lifestyle habits (ARNOLD et al., 2016). It is evident that a nutritional transition is occurring around the world, mainly affecting developing countries. Thus, lifestyle risk factors are

modifiable and include: alcohol consumption, low fruit and vegetable intake, high consumption of red meat and processed foods, obesity, smoking and physical inactivity (HARRISS et al., 2009; FEDIRKO et al., 2011; WALTER, 2014; BOUVARD et al., 2015). CRC is one of the most malignant tumors in both sexes, among all types of tumors worldwide (HUANG et al., 2016).

2.1.1 Risk factors

Risk factors are conceptualized as any action that increases the risk of an individual developing a certain disease or suffering a certain disease (BRASIL, 2003).

Risk factors for the development of CRC can be considered: age over 50 years; first degree relatives with intestinal cancer; genetic syndromes (family adenomatous polyposis and nonpolyphoid hereditary colorectal cancer); inflammatory bowel disease (ulcerative colitis, Crohn's disease); excessive consumption of alcoholic beverages and animal fat; smoking and obesity (BRASIL, 2003).

2.2 Technology Mapping

Patentometry is a tool used for quantitative and qualitative analysis, i.e., the technological mapping of patents (ANDRADE, 2014; ANTUNES et al., 2018).

Abbas, Zhang and Khan (2014) conducted a review of the patent literature and concluded that patent analysis is a tool that can be used to forecast technological trends. Petentometry is one of the instruments capable of evaluating and monitoring the transformations and technological growth is the analysis of patents (PANTANO et al, 2017).

3. Methodology

In this study, a mapping of the technologies related to colorectal cancer was performed (ARNOLD et al, 2016; ANTUNES et al., 2018). The search took place during the months of May and June 2019. It was used the Leans database, which captures global information on patents and academic research, available through the link: https://www.lens.org.

The search for information occurred through the term "colorectal cancer", inserted in the title or abstract fields of the base. Patents with publication date between January 1, 2000 and June 1, 2019 were selected. Only patents granted and patents deposited (patent application and granted patent) were filtered for analysis. Lens allows the analysis of patent and scientific information (articles, dissertations, theses, among others) of a certain area. Thus, it enables a more effective and comprehensive analysis of the context of a technology. Thus, in the first stage of the research, we proceeded with the analysis of patent information: year of publication, countries, inventors, holders and International Classification of Patents (IPC). Then the information of the academic works cited in the patents were mapped: authors, institutions, journals, countries and subjects of the works.

The search expression and the number of records identified are shown in Table 1:

Table 1 - Search expression used in the study.

Search expression *	Number of records	
	Patent	School work
title:("colorectal cancer") OR abstract:("colorectal cancer")	6.850	14.083

*Filters: Publication Date = (Jan 1, 2000 - Jun 1, 2019) types = (Patent Application , Granted Patent)

Source: research data (2019).

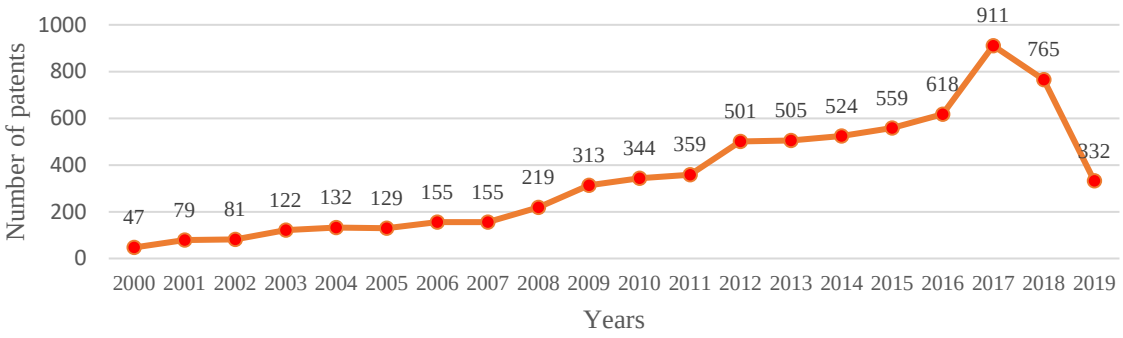
4. Results

In the following items are presented the results regarding the mapping of patents on colorectal cancer and the mapping of academic works cited in these technologies.

4.1 Patent Mapping Related to Colorectal Cancer

6,850 patents related to colon and rectal cancer were identified. 5,445 (79.48%) correspond to patents filed and 1,405 (20.51%) are patents granted in the period from 2000 to 2019. The evolution of the publication of these patents occurred as shown in Figure 1.

Figure 1 - Patents on colorectal cancer by years (2000-2019).



Source: research data (2019).

In 2000, the first year of the historical series, 47 patents on colorectal cancer were published. The growth in the number of technologies deposited and granted was constant. In 2017 there were a total of 911 deposits, indicating a growth of 1938.29% in relation to the year 2000. The first identified patent of the period was "Apc Mutation Associated With Familial Colorectal Cancer In Ashkenazi Jews" - APC gene mutation associated with colorectal cancer in families of Ashkenazi Jews (LAKEN et al., 2000), developed by Steve Laken, Stephen Gruber, Gloria Petersen, Kenneth Kinzler and Bert Vogelstein. This patent belongs to Johns Hopkins University, located in Baltimore, Maryland, USA.

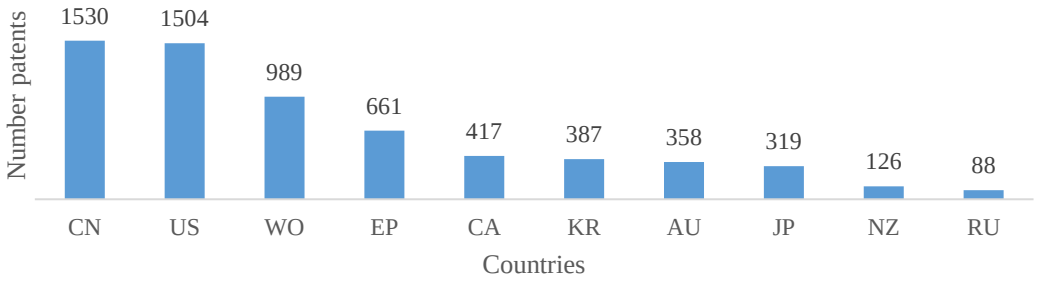
The patent is described as follows:

> During routine screening of a patient with a family history of colorectal cancer for truncation of APC mutations, a new missense mutation was identified. After further evaluation, it was found that 6% of ashkenazi Jews carry this mutation, and that it was present in the DIFFERENCE 20% of ashkenazis with a family history of CRC. Probes, methods and kits are provided to identify individuals affected

by this missense mutation (LAKEN et al., 2000).

The Figure 2 shows the distribution of patents analyzed by country.

Figure 2 - Patents on colorectal cancer by country (2000-2019).



Note: CN - China; US - United States of America; WO - World Intellectual Property Organization; EP - European Patent Organization; CA - Canada; KR - Republic of Korea; AU - Australia; JP - Japan; NZ - New Zealand; RU - Russian Federation.

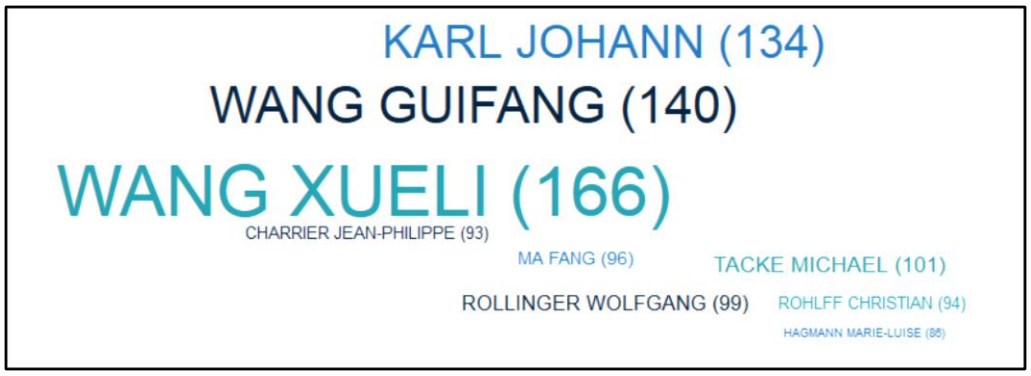
Source: research data (2019).

Among the countries that have developed the most technologies related to colorectal cancer is China, with 1530 patents and the United States, with 1504 documents. This result is related to the large amount of research that both countries have developed on color and rectal cancer, especially the United States.

Other countries that have stood out in the technological production of the area are Canada, Korea, Australia, Japan, New Zealand and Russia.

The figure 3 shows a cloud of the inventors of the patents analyzed in this work.

Figure 3 - Patents on colorectal cancer by inventors (2000-2019).



Source: research data (2019).

Wang Xueli was the most outstanding inventor in this ranking, with 166 patents identified. His patents were applied for by Yinchuan Shanghetu New Tech Dev Co Ltd, being initially applied for in China.

Other outstanding inventors are Wang Guifang, also from China, with 140 patent documents, and Karl Johann, with 134. He has patents predominantly filed in Canada and the United States, and there are also deposits in other countries. Figure 4 shows the holders of patents on colorectal cancer.

Figure 4 - Patents on colorectal cancer by holders (2000-2019).

Note - The map shows the logos of the following institutions: Oxford Biotherapeutics Ltd, Thomas Jefferson University, The Johns Hopkins University, Roche Diagnostics Operations Inc, Roche Diagnostics Gmbh, Genomic Health Inc, Oncotherapy Science Inc, Biomerieux, Exact Sciences Corporation, Biomerieux e Nsabp Foundation Inc.

Source: research data (2019).

With regard to the holders of patents on colorectal cancer, it appears that the universities of Oxford, Thomas Jefferson and The Johns Hopkins are the ones that stand out the most. It is noteworthy that the three institutions are located in the United States, which is related to the supremacy of the country in technological production in this area. Table 2 presents the International Classifications that most have patent documents on colorectal cancer.

Table 2 - Patents on colorectal cancer by international classification (2000-2019).

Classification IPC	Description	N° of patents
A61P35/00	Human needs section, referring to medical or veterinary science/hygiene, related to the specific therapeutic activity of chemical compounds or medicinal preparations from antineoplastic agents;	2140
C12Q1/68	Section of chemicals or metallurgy, referring to biochemistry, beer, alcohol, wine, vinegar, microbiology, enzyme, genetic engineering or mutation, related to measurement or testing processes involving enzymes, nucleic acids or microorganisms (g01n 33/53 immunoassays), their compositions or their test papers, processes for preparing these compositions, responsive control to environmental conditions in microbiological or enzymatic processes, specifically in measuring or testing processes involving enzymes, nucleic acids or micro-organisms (measuring or testing apparatus or means of measuring or detecting environmental conditions, p. e.g. colony counters, c12m 1/34), compositions for this purpose or preparation processes of such compositions involving nucleic acids.	1989
G01N33/574	Section referring to Physics for measurement or testing, specifically for investigation	1731

	or analysis of materials by determining their chemical or physical properties (measurement or test processes, other than immunological assays, involving enzymes or microorganisms c12m, c12q), for investigation or analysis of materials by specific methods not covered by groups g01n 1/00-g01n 31/00, for cancer.	
A61K39/395	Human needs section, focused on medical or veterinary science and/or hygiene, specifically related to preparations for medical, dental or hygienic purposes (devices or methods specially adapted to give pharmaceutical products determined physical forms or for their administration A61J 3/00; chemical aspects of, or use of, bandaging materials, dressings, absorbent pads or A61L surgical articles; C11D soaps), within the scope of medicinal preparations containing antigens or antibodies (G01N 33/53 immunoassay materials) with antibodies (A61K 38/36 agglutinins), immunoglobulins, immunosorum, p. e.g. antilymphocytic serum.	516

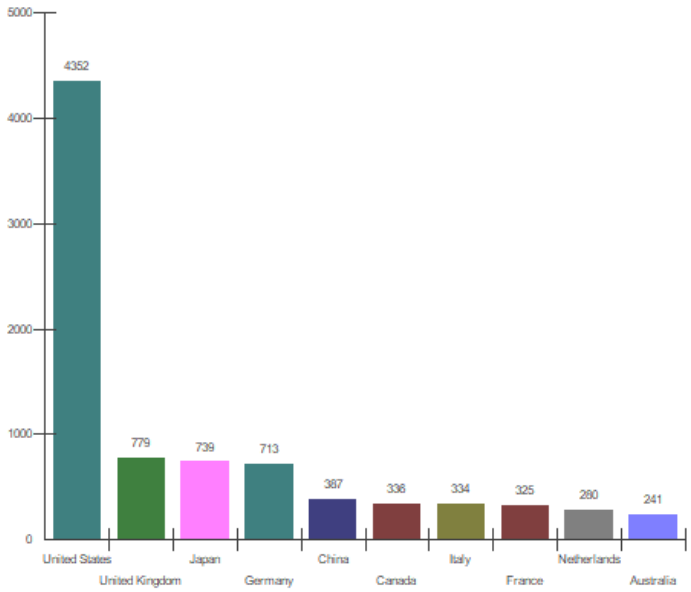
In general, patents in this area are classified in the human needs, chemical or physical sections. This is related to the nature of the technologies developed to combat the problem, which generally include machines or equipment to diagnose the problem or even to treat it. In addition, it is related to the remedies used throughout the treatment process.

4.2 Patent mapping related to colorectal cancer

The analysis of academic papers cited in patent documents is important for understanding the evolutionary context of a given technology. In this sense, this section shows some information regarding the mapping of the scientific papers cited in the patents analyzed in the research.

The figure 5 shows the academic works cited by patents related to colorectal cancer by country (2000-2019).

Figure 5 - Academic papers cited by patents related to colorectal cancer by country (2000-2019).

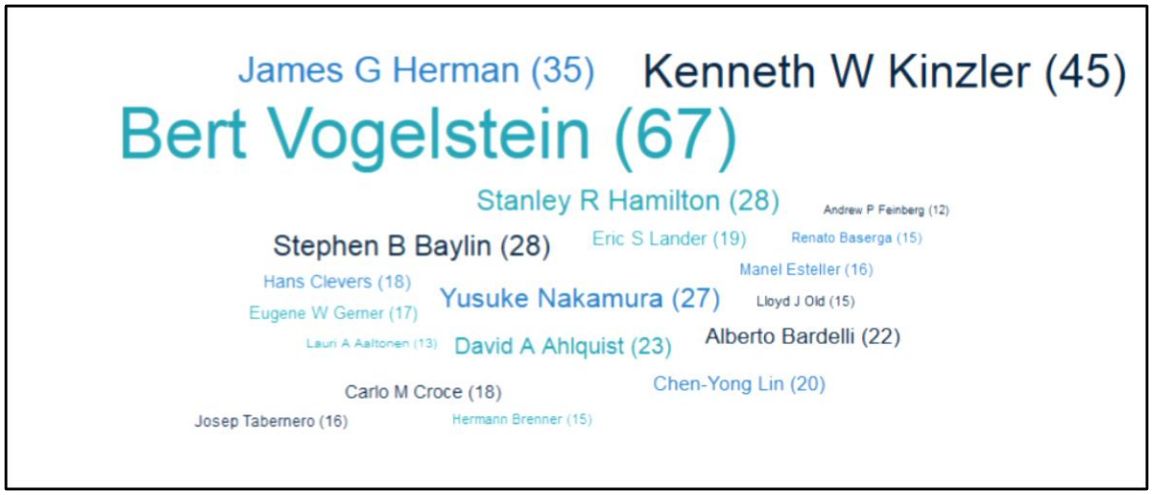


Source: research data (2019).

The United States stands out as an isolated country producing academic works on colorectal cancer, with 4,532 articles identified. This aspect is closely related to the prominence of the country in technological production (patents), as previously presented.

Other countries that have presented considerable scientific production are the United Kingdom, Japan and Germany. China is not one of the countries with the greatest prominence in the ranking, but has important scientific production in the area, which also has a relationship with the country's technological production. Figure 6 shows the map of authors of these works.

Figure 6 - Academic studies cited by patents related to colorectal cancer by authors (2000-2019).

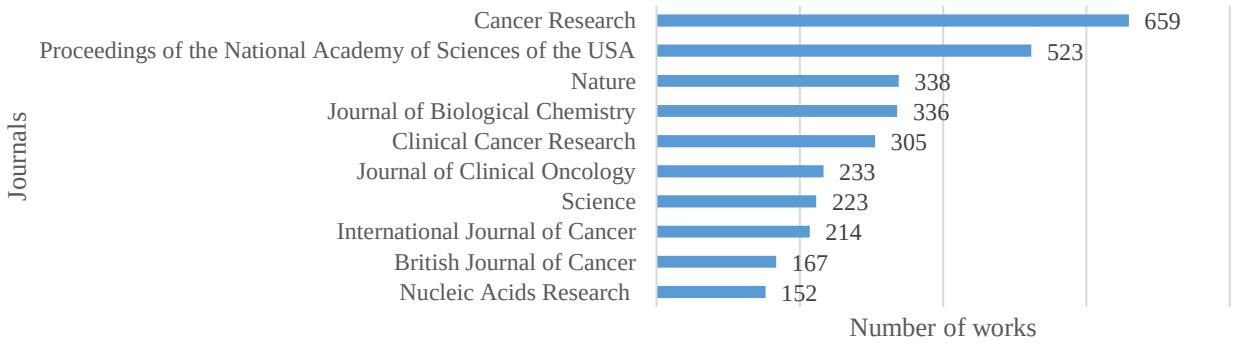


Source: research data (2019).

Doctor Bert Vogelstein is the researcher with the highest volume of work on the subject, with 67 documents identified. Kenneth Kinzler and James G. Herman also have a large amount of research on the subject, with 45 and 35 papers, respectively.

The three researchers are North Americans. Two of them have already established some link with Johns Hopkins University (one of the institutions with the highest number of patents on colorectal cancer in the world). The figure 7 shows the journals in which the studies under analysis have been published (2000-2019).

Figure 7 - Academic works cited by patents related to colorectal cancer by periodicals (2000-2019).



Source: research data (2019).

Cancer Research has 659 of the publications cited by patents on colorectal cancer. It is a journal published by the American Association for Cancer Research and was created in 1941. It has an impact factor of 9.13 and ranks 17th in the ranking of journals on oncology in the world, among 222 journals. The figure 8 shows the map of the institutions originating from these academic works.

Figure 8 - Academic studies cited by patents related to colorectal cancer by institutions (2000-2019).

Figure 8 - Academic studies cited by patents related to colorectal cancer by institutions (2000-2019).

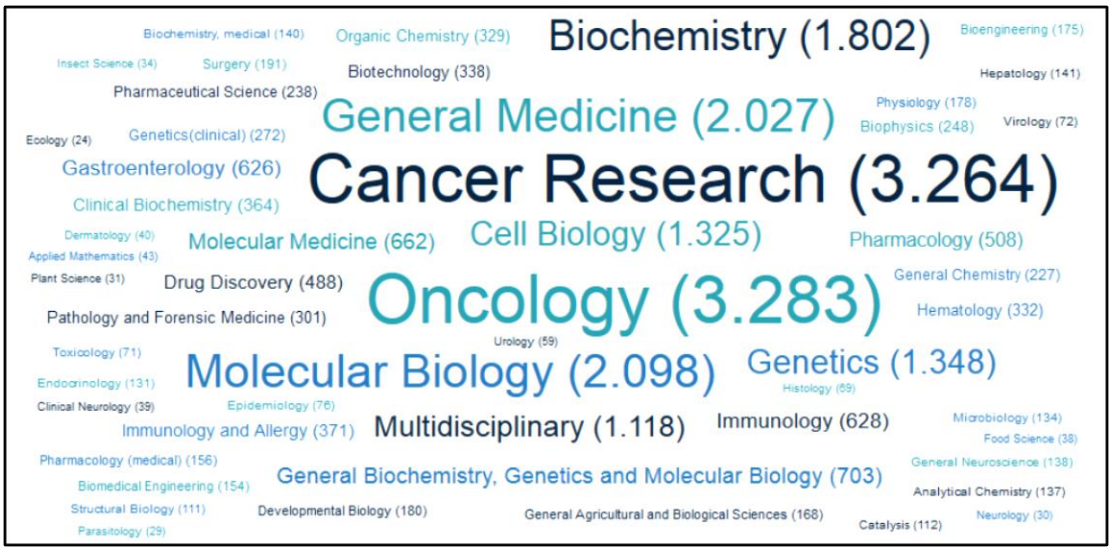
Note - The map shows the logos of the following institutions, respectively: Harvard University, National Institutes of Health, Johns Hopkins University, University of Texas MD Anderson Cancer Center, Memorial Sloan Kettering Cancer Center, Mayo Clinic, University of Michigan, University of California, em San Francisco, French Institute of Health and Medical Research e Max Planck Society.

Source: research data (2019).

Among the universities that have produced the most research cited in the patents on colorectal cancer are Harvard University, the National Institutes of Health and Johns Hopkins University. The three institutions are located in the United States, which contributes to the country's numbers in technological production in the area.

In addition, it is also observed that Johns Hopkins has great know-how in the subject, both in scientific production and in technological production (patents). Figure 9 shows the cloud of the main issues identified in the researches.

Figure 9 - Subjects addressed in academic works cited by patents related to colorectal cancer (2000-2019).



Source: research data (2019).

Among the main expressions are "cancer research", "oncology", "molecular biology", "general medicine" and "biochemistry". In general, these are terms aimed at medicine and oncology, specifically involving studies on cancer and on possible alternatives to the problem.

5. The Final Considerations

From the mapping of patents carried out in this study, in the period from 2000 to 2019, it was found that in 2017 there was a total of 911 applications, indicating a growth of 1938.29% in relation to the year 2000. The first patent identified in the period was "Apc Mutation Associated With Familial Colorectal Cancer In Ashkenazi Jews" - APC gene mutation associated with colorectal cancer in families of Ashkenazi Jews. Among the countries that have developed the most technologies related to colorectal cancer is China, with 1530 patents and the United States, with 1504 documents. Wang Xueli was the most outstanding inventor in this ranking, with 166 patents identified. His patents were applied for by Yinchuan Shanghetu New Tech Dev Co Ltd, being initially applied for in China.

As for the academic papers cited by patents related to colorectal cancer by countries (2000-2019), the United States stands out as an isolated country producing academic papers on colorectal cancer, with 4,532 articles identified.

Doctor Bert Vogelstein is the researcher with the highest volume of work on the subject, with 67 documents identified. The journal Cancer Research has 659 of the publications cited by patents on colorectal cancer.

It is important to note that the universities that have produced the most research cited in the patents on colorectal cancer are Harvard University, the National Institutes of Health and Johns Hopkins University. Given the high prevalence of this disease, there is a need for a greater incentive in scientific and technological research to reduce it and improve the quality of life of patients affected by this type of cancer.

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