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Patentometric Analysis of TB Vaccines using subject classification : a Case Study of the Technical Status of a Technological Domain

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Abstract:	The main goal of the research is to perform an informetric analysis of a set of patents, weighing up the international classification inside the units of analysis and measurement of the study, to obtain a better diagnosis of the composition of the technical status in technological domains. The results will allow diagnosing the productivity indexes which analyze sudden changes in the production levels and its correlation with scientific advances and the main epidemiological events; the science-technology relationship and emerging technological developments. Also the collaborations, citations and technological specialization by area have been mapped. The data for the informetric analysis are obtained from the granted patents database of the United States, using a proposed work methodology and set of techniques and indicators based on the tool proINTEC. This research will enhance future patent studies by contributing with the work methodology, the application of complex patent indicators; the use of the classification field as the analysis unit in studies of technological domains and the analysis of the technical status in prophylactic areas of biotechnology.
Response to Reviewers:	As requested by the reviewers we have made major revisions to the paper by elaborating/emphasizing on the scientific and methodological approach and improving the English language (the text originally was written in Spanish). While it still, of course, remains a case-study, we believe now to fit better with the aims of a scientific journal and expectations of scholar readers. We have asked two more authors to join in order

	to raise the academic and theoretical status of the paper, which now better reflects the standards of scientific collaboration in Latin America on the subject.

Patentometric Analysis of TB Vaccines using subject classification : a Case Study of the Technical Status of a Technological Domain

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Introduction

Patents are a technological indicator of significant relevance in studies of technological innovation (Basberg 1982, 1983; Pavitt 1985; Grupp, Schmoch and Kuntze 1991; Narin 1995), and one of the most reliable data sources for bio-informetric studies in the last decades (Díaz-Pérez and Moya 2008).

Schmookler was the precursor of the use of patents as a technological indicator in a paper of 1966. A patent is a measure of scientific-technological productivity. It is a document which communicates the scientific advance like journal articles; indicating also that the resulting technology can be applied in production processes, allowing a better performance in the transfers of technologies and licenses. The bibliometric indicators comprise the patentometric studies (patent indicators) (Narinand Olivastro 1988; Narin 1994; Bordons and Zulueta 1999; Spinak 1998; González-Albo and Zulueta-García 2007; Haupt *et. al.* 2007; Corrocher *et. al.* 2007; Martínez-Méndez *et.al.* 2010;Klitkou and Gulbrandsen 2010; Pao-Long, Chao-Chan and Hoang-Jyh 2010).

Because of the potential use of the patent document, biotechnology has chosen patentometric studies as one of its main research instruments to monitor the current status and future trends of science, to identify emerging technologies and new fields of application of science in technology (Bhattacharya and Patra 2009). Nanotechnology is one of the scientific domains that demonstrates the relevance of patent analysis (Meyer and Persson1998; Hullmann and Meyer 2003; Meyer2000, 2001, 2006; Huang *et. al.* 2005; Sheu *et. al*. 2006;Hullmann 2007; Bonaccorsi and Thoma 2007), mainly the area of nanotubes (Kuusi and Meyer 2007; Gupta and Pangannaya 2000; Pao-Long, Chao-Chan and Hoang-Jyh 2010), showing the relevance of patent metric studies in high impact areas (Li, Chen, Huang and Roco 2007; Leydesdorff and Heimeriks 2001; Leydesdorff 2008_a; Pei-Chun, Hsin-Ning, and Feng-Shang 2010).

Despite the importance of patent studies, most of patent analysis use frequency counts by years, countries, assignees and inventors, while patentometric studies making analysis with a subject classification remain scarce.

As stated by the norms established by the World Intellectual Property Organization (WIPO), every invention must be attributed one or several classifications in the field number 51 of the patent document. These classifications should identify and describe which areas of the technical knowledge the invention belongs to.

The International Patent Classification (IPC) comprises the set of knowledge that can be considered to be included in the scope of invention patents. As it is a unique and international system, it achieves a standardization in the taxonomies of the technological knowledge. It includes not only the bigger classes and categories by disciplines, but also even the deepest complexity levels of each subject, reaching almost to describe the proper results.

The hierarchical levels of the last version (eighth edition) of the IPC with its full structure of symbols contains: 8 sections, 129 classes, 633 subclasses, 7066 groups and 10047 subgroups. This wide subject coverage is what allows to perform metric analysis with this field of the patent document.

This research shares the criteria that the analysis by classification allows to perform a better mapping to represent the underlying science in patent documents (Tijssen 1992; Leydesdorff 1987; Leydesdorff and Vaugman 2005; Jaffe and Trajtenberg 2002; Leydesdorff 2004; Porter and Cunningham 2005). It also allows to know the subject specialization by country, region and institutes (van Zeebroeck *et. al*. 2006; Fall *et. al*. 2003; Cong and Han-Tong 2010).

The IPC can be used as the analysis unit to explore the information contained in patents (Dibiaggio and Nesta 2005); and it can be even compared to the subject categories that the ISI attributes to journals, according to Leydesdorff. This author trusts the classification classes as equivalents to those of the journals, proposing to analyze the corresponding equivalent of a citation matrix between journal and journal (Leydesdorff 2008_b). Having these previous ideas in mind, this study proposes the use of the IPC as another analysis unit beyond the application of the traditional patent indicators.

The research has as a main goal to perform an informetric analysis of a set of patents, weighing up the international classification as another unit of analysis and measurement in the study, to obtain the diagnosis of the composition of the technical status in technological domains.

Methodology and Procedures

The methodology of this research, which was tested in previous researches with relevant results (Díaz-Pérez and Moya-Anegón 2008; Díaz-Pérez 2009; Giráldez, Díaz-Pérez and Armas 2008; Díaz-Pérez, Rivero and Moya-Anegón 2010), is explained in the following paragraphs.

Database choice:

The data source selected is the United States Patents and Trademarks Office, using specifically the granted patents database, because of the rich set of work possibilities and rigorous invention examination process (Pavitt 1988; Michel and Bernd 2001; Trilateral Cooperation 2005; Borja González and Zulueta

2007). In this database most of the candidate TB vaccines existing today under clinical trial can be found, according to the official website Stop TB Partnership Working Group on New TB Vaccines.

Search strategy:

The search strategy was to interrogate the USPTO database on patent records granted between January 1st, 1976 and December 31, 2011, where words starting with the strings “Tuberculosi" and "Vaccin” occur in the fields Title, Abstract and Claims. The truncation operator was used to cover all the possibilities of apparition of these terms.

Strategy: (ttl/tuberculosi$ and ttl/vaccin$) or (abst/tuberculosi$ and abst/vaccin$) or (aclm/tuberculosi$ and aclm/vaccin$).

184 patents granted by the USPTO about TB Vaccines were retrieved.

The date retrieved corresponds to the year the patent was granted, considering it more relevant as it means newly constituted knowledge and innovations with trade opportunities.

The time span (and limitation) corresponds to the sample selected by the International Development Project – Application of Analysis and Visualization Technologies of Biomedical Data of the Scientific and Technological Cooperation Program between Cuba (CITMA) and Mexico (CONACYT).

Analysis unit:

Patents are considered units of technological capacity because they represent technological knowledge, being used as units of study, computing and measurement of a domain. The bibliographic data obtained is grouped by time, subject and geographical variables.

Data-processing:

The tool used to download, normalize, process, analyze and visualize the data is the software proINTEC (Díaz-Pérez and Moya-Anegón 2008; Díaz-Pérez, Rivero and Moya-Anegón 2010; Moya- Anegón, Chinchilla, Corera and Díaz-Pérez 2011).

Indicators of bibliometric origin were used but adapted in this case to the characteristics of patent documents. The next lines show the equations of the complex indicators being used:

$$\mathrm{CPAPT} = \Pi_{\Im_{count(patent)},date,country}(PATENTS \bowtie ASSIGNEES \bowtie COUNTRIES)$$

Indicator CPAPT=Amount of patents by year by country of the assignee

$$\mathrm{CPPT} = \Pi_{\Im_{count(Assignee)},country}(ASSIGNEES \bowtie COUNTRIES)$$

Indicator CPPT=Amount of patents by country of the assignee

$$\mathrm{CPPI} = \Pi_{\Im_{count(Inventor)},country}(INVENTORS \bowtie COUNTRIES)$$

Indicator CPPI=Amount of inventors by country of the inventor

$$\text{CPAPI} = \Pi_{\Im_{count(patent)},date,country}(PATENTS \bowtie INVENTORS \bowtie COUNTRIES)$$

Indicator CPAPI=Amount of patents by year by country of the inventor

$$\text{CPIPI} = \Pi_{\Im_{count(patent)},inventor,country}(PATENTS \bowtie INVENTORS \bowtie COUNTRIES)$$

Indicator CPIPI=Amount of patents by inventor by country of the inventor

$$\text{CPTPT} = \Pi_{\Im_{count(patent)},assignee,country}(PATENTS \bowtie ASSIGNEES \bowtie COUNTRIES)$$

Indicator CPTPT=Amount of patents by titular by country of the assignee

$$\text{CPTC} = \Pi_{\Im_{count(patent)},assignee1,assignee2}(PATENTS \bowtie ASSIGNEES1 \bowtie ASSIGNEES2)$$

Indicator CPTC=Amount of patents by joint assignees

$$\text{CPIC} = \Pi_{\Im_{count(patent)},inventor1,inventor2}(PATENTS \bowtie INVENTORS \bowtie INVENTORS)$$

Indicator CPIC=Amount of patents by joint inventors

$$\text{CPCIPs} = \Pi_{\Im_{count(patent)},section}(PATENTS \bowtie CLASSIFICATION)$$

Indicator CPCIPs = Amount of patents by IPC [section]

$$\text{CPPT}_{Section=A} = \Pi_{\Im_{count(Assignee)},country}(\sigma_{section=A}(ASSIGNEES \bowtie COUNTRIES \bowtie CLASSIFICATION))$$

Indicator $\text{CPPT}_{\text{Section=A}}$=Amount of patents /section A by country of the assignee

$$\text{CPA}_{Section=A} = \Pi_{\Im_{count(patent)},date}(\sigma_{section=A}(PATENTS \bowtie CLASSIFICATION))$$

Indicator $\text{CPA}_{\text{Section=A}}$=Amount of patents / section A by year

$$\text{CPPT}_{Section=C} = \Pi_{\Im_{count(Assignee)},country}(\sigma_{section=C}(ASSIGNEES \bowtie COUNTRIES \bowtie CLASSIFICATION))$$

Indicator $\text{CPPT}_{\text{Section=C}}$=Amount of patents /section C by country of the assignee

$$\text{CPA}_{Section=C} = \Pi_{\Im_{count(patent)},date}(\sigma_{section=C}(PATENTS \bowtie CLASSIFICATION))$$

Indicator $\text{CPA}_{\text{Section=C}}$=Amount of patents / section C by year

$$\text{CPPT}_{Section=G} = \Pi_{\Im_{count(Assignee)},country}(\sigma_{section=G}(ASSIGNEES \bowtie COUNTRIES \bowtie CLASSIFICATION))$$

Indicator $\text{CPPT}_{\text{Section=G}}$=Amount of patents /section G by country of the assignee

$$\text{CPA}_{Section=G} = \Pi_{\Im_{count(patent)},date}(\sigma_{section=G}(PATENTS \bowtie CLASSIFICATION))$$

Indicator $\text{CPA}_{\text{Section=G}}$=Amount of patents / section G by year

$$\text{CPA}_{Section=G} = \Pi_{\Im_{count(patent)},subclass1,subclass2}(PATENTS \bowtie CLASSIFICATION1 \bowtie CLASSIFICATION2)$$

Indicator $\text{CPA}_{\text{Section=G}}$=Amount of patents / section G by year

$$\text{CCT} = \Pi_{\Im_{count(referencing\_patent)},assignee}(PATENTS \bowtie REFERENCES \bowtie ASSIGNEES)$$

Indicator CCT=Amount of citations by assignee

Techniques:

Among the techniques for data visualization, the tabular form is used, through frequency counts in fields of patents, diagrams, matrixes to visualize patent data through crossed variables; as well as networks presented in the form of nodes or vertices, where the semantic structure is defined by the links connecting these nodes. This last technique shows the patent analysis through technological maps, defining the visual representations of the status of the domain, presenting graphically the results of the analysis in a synthesized form.

The visualization through networks makes it possible to represent the network links crossing variables to find in this case, behaviors in the set of patents (joint assignees and inventors and linked subject areas). Metric studies constitute a strong field of application for network techniques (Van Raan and Peters 1989; Courtial and Callon 1991; Van Raan and Tijssen 1993; Verspagen 2007; Perianes-Rodríguez, Olmeda-Gómez and Moya-Anegón 2010). In this case it is used the analysis of patent networks is used because it allows to group patents by common characteristics in those critical fields of analysis, identifying behaviors. Also, network analysis help the researcher to intuitively comprehend the whole data structure of the domain under study (Yoon and Park 2004).

For a better representation of the information we used the Pathfinder pruning algorithm, widely used in other studies (Moya-Anegón *et. al.* 2004; Guerrero-Bote *et. al.* 2006; Vargas-Quesada and Moya-Anegón 2007) because it allows to show only the more relevant links in the network. It is also used as a pruning technique, the numerical limitation of the intensity of relationships in those nodes with few links. To distribute the nodes in the visualization of the domain, the Springs Embedded spatial representation algorithm is used, with the help of Netdraw to manipulate the graphs in the visual representations.

Results and Discussion

Case study: Tuberculosis Vaccines

Tuberculosis (TB) is one of the most prevalent and mortal infectious diseases (Aagaard, Dietrich, Doherty and Andersen 2009). An estimate states that 1/3 of the world population is infected by Mycobacterium tuberculosis (M. tuberculosis) and therefore subject to develop the disease. According to the World Health Organization, every year around ten millions of cases and two millions of deaths are notified, being the first cause of death in patients with the Acquired Immuno Deficiency Syndrome (AIDS).

There is only one vaccine available to prevent it, the Bacillus Calmette Guérin (BCG) (Calmette and Guérin 1905,1909), but it induces an extremely variable protection (Mohd-Nor, Acosta and Sarmiento 2010). The effectiveness of the BCG vaccine has been assessed in several populations. For instance in a study which took as the sample a native population in North America, it reported an index of 80% of protection. However in another notable study performed in South India during the 60' and 70', its protective effect was not present (Martin, Bigi and Gicquel, 2007). Although the BCG has shown an impact against the most deadly forms of the disease during the childhood, it is debated its effectiveness in the prevention of the Lung Tuberculosis in adults (form responsible for the biggest transmission of the disease) and in the reactivation from infected individuals (Hesseling et. al. 2007). It has been also proved that the protective effect of the BCG has a decreasing behavior and therefore it is temporary (10-20 years) (Aagaard, Dietrich, Doherty and Andersen 2009).

The World Health Organization (WHO) released in 1992 a report warning the world about the potential risk of this epidemic disease, based on its reemergence in countries already infected, and its appearance in developed countries where it was not present before. Accordingly the WHO announces a World Emergency about Tuberculosis.

Productivity by years and countries

The time series obtained evidence a notorious quantitative change in the rate of production of patents in the decade of the nineties. During 21 years, between 1976 and 1997, only 9 patents were granted. However, in the year 1998, 10 patents were granted and from there on, until 2011, the production rate remained in between 4 and 18 patents per year, with a mean of 11 patents per year (Fig. 1).

The production of 2011 contrasts with the behavior during the period of 1998-2010, being granted 33 patents in this year. That means an increase of the 300% related to the mean production value of the preceding 13 years.

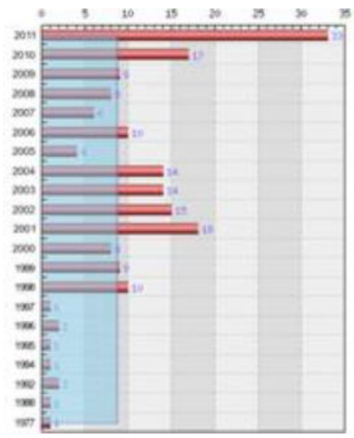


Fig. 1: Patents by year in TB Vaccines
Source: Software proINTEC

This notorious increase in the productivity rate has the precedent of the apparition of the AIDS disease, because it causes the death of a high number of people infected by tuberculosis. This situation allowed the reemergence of TB even in very developed countries where the disease was not present before. It was a key factor for bigger economical investments to support the scientific research, and propitiated the World Health Organization (WHO) declaration of the world-wide emergency on tuberculosis in 1992.

Also this increase in the late nineties, sustained during the first decade of the new century, is correlated in time with significant biotechnological advances and scientific findings: new technologies for sequencing biological macromolecules, the development of microarray analysis techniques, the publication of the

Genome Sequence of Tuberculosis in the prestigious journal *Nature* (Cole, *et. al.*, 1998); new DNA (Lozes *et. al.*, 1997; Denis *et. al.*, 1998; Baldwin *et. al.*, 1999; Li Z *et. al*, 1999).

The patentometric analysis by country shows the following scheme of development of TB Vaccines: United States (95 patents) in the first place, which corresponds to the great number of research centers focused on its study, followed by France (15 patents) and United Kingdom (12 patents), being both, countries with a great technological development in this subject area; followed by Denmark, Germany, and Belgium (Table I). Despite the severe danger which Tuberculosis means to humanity, only 21 countries figure as holders of registered inventions in the USPTO.

India and Japan have only 2 granted patents in the USPTO respectively, despite having a relatively high prevalence of cases of the disease (Mori, 2000; WHO, 2009). For instance, India has the fifth part of its population infected by Tuberculosis, according to the *WHO Official Says*. Every year two million people develop the active TB more than in any other country in the world.

This study proves that the technological productivity in terms of patents by countries does not correspond to the severity in which this disease affects them (number of deaths and infections by TB). The same happens with the scientific productivity, the countries with the higher productivity of articles are not the countries with a high incidence of cases of TB, according to a recent study on the subject (Guzmán, Carrillo and Jiménez 2010).

On the other hand, the behavior of the patent-holdership indeed corresponds to the productivity by country (Fig. 2). The US has 43 assignees in the USPTO with an average of one patent by assignee. With a similar average, it is followed in number of assignees by the UK with 7. France, that has the second position in the ranking of total production by country have registered 15 patents with 4 assignees.

Outstandingly, with a single holder, Denmark and Belgium have 9 and 7 registered patents respectively, while Germany and Canada with a lower number of patents have a bigger number of assignees developing its researches.

Because of its relevance, the group of researchers by country working in this subject was analyzed (Fig.3).

In United States, 132 researchers have worked in inventions related to TB Vaccines, in France 33 and in the United Kingdom 31. This movement of researchers corresponds to the technological development in these leading countries, owning the source of the protected knowledge and the main scientific potential integrating the research front in TB Vaccines.

Table 1: Patents by year and country of assignee
Source: proINTEC

Conntries(Assig)/Years	1988	1992	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Total
UnitedStates of America		**2**	**1**	**1**	**1**	**6**	**3**	**5**	**11**	**8**	**8**	**9**	**1**	**4**	**3**	**5**	**4**	**8**	**15**	95
France						**1**	**2**	**1**		**4**		**1**	**1**	**1**	**1**				**3**	15
United Kingdom (Great Britain)	**1**								**2**	**2**	**1**			**1**			**1**	**2**	**2**	12
Denmark							**1**	**1**			**1**			**2**				**1**	**3**	9
Belgium						**1**	**2**				**2**			**1**	**1**					7
Germany											**1**	**3**						**2**	**1**	7
Canada									**3**		**1**						**1**			5
Korea, Republic of						**1**									**1**				**2**	4
Australia																**1**			**2**	3
Sweden													**2**						**1**	3
India												**1**					**1**			2
Israel																			**2**	2
Italy									**1**									**1**		2
Japan																		**2**		2
Switzerland														**1**					**1**	2
China																	**1**			1
Finland																	**1**			1
Iceland							**1**													1
Netherlands																			**1**	1
New Caledonia									**1**											1
Spain																**1**				1
Total	1	2	1	1	1	9	9	7	18	14	14	14	4	10	6	7	9	16	33	**176**

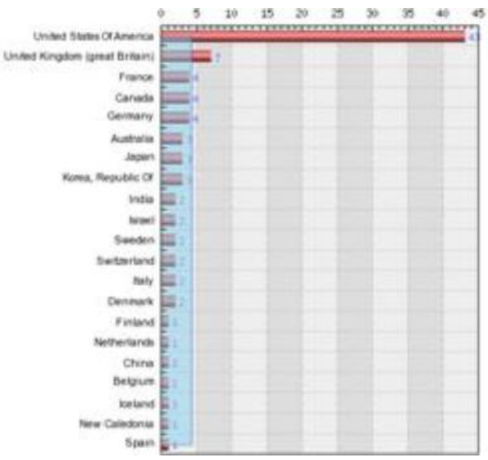


Fig. 2: Amount of assignees by country of the assignee
Source: proINTEC

They are followed in number of researchers by country by: Germany (17), Denmark (17), Canada (11) and Korea (16 researchers).

An interesting point in this analysis is the representation of China with 19 researchers, occupying one of the first positions in the graph of countries of inventors (Fig. 3). This shows their scientific potential in terms of human resources focused on researching TB Vaccines, even when it does not appear as an assignee in the patents of USPTO.

It is important to highlight how researchers from Russia, Estonia, Austria and Mexico are also among the current research front in TB Vaccines even when their countries are not included as assignees in the USPTO (Fig. 3).

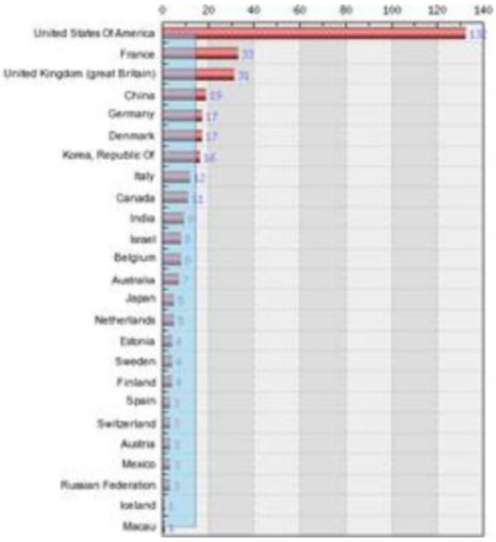


Fig. 3: Amount of Inventors by country of the Inventor
Source: proINTEC

Productivity by Inventors and Assignees

The kernel of researchers in the creation of technology related to TB Vaccines within the USPTO consists of 359 inventors. There are 184 granted patents, giving us a yearly average of almost 2 patents per inventor during the period 1976-2011. There is a group of 21 inventors that have participated in the creation of more than 5 patents granted by USPTO (Fig. 4).

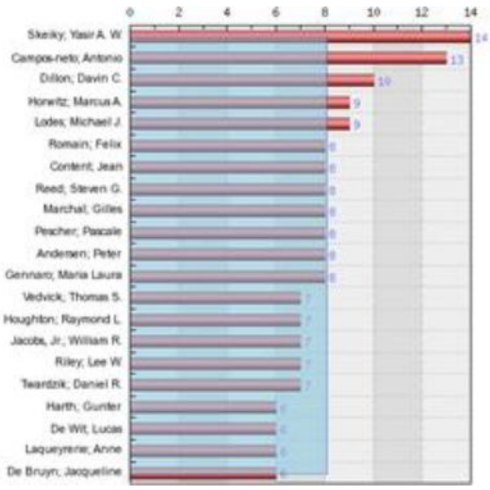


Fig. 4: Main Inventors (more than 5 patents)
Source: proINTEC

Analyzing the inventive activity of the discipline by year to identify the inventors who work on the TB Vaccines subject more consistently, we found that there are 41 researchers to whom more than 1 patent was granted in one year. Table II identifies the main researchers currently working more systematically in prophylactic alternatives against TB. The table also shows that the inventive activity by inventor has increased after year 1999 where inventors with 2 patents about TB Vaccines in a year can be seen.

Table 2: Patents by Inventors by Year (more than 1 patent in a year)
Source: proINTEC

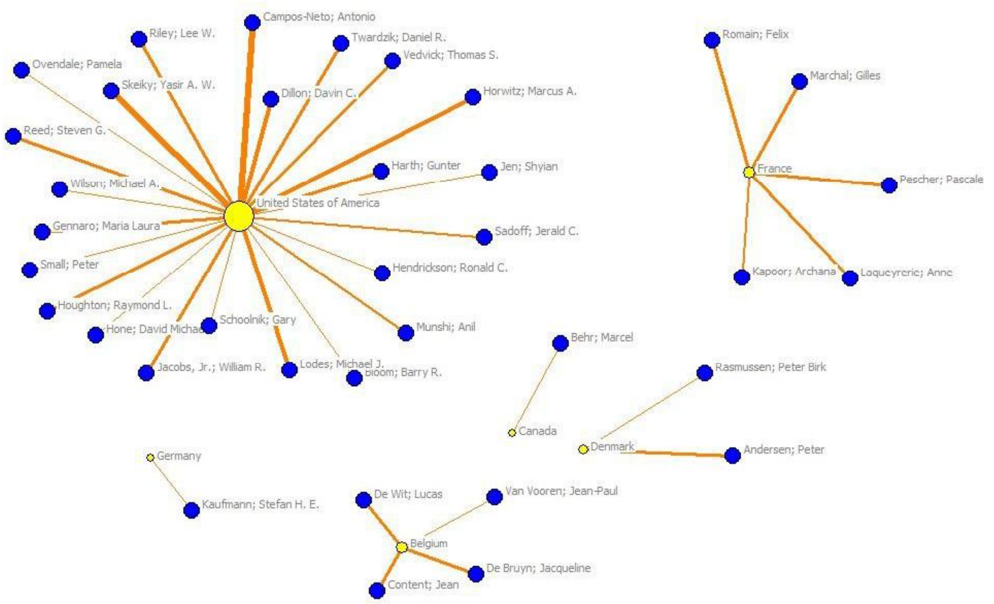
Inventors/Years	1999	2001	2002	2003	2004	2005	2006	2009	2010	2011	Total
Campos-Neto; Antonio				**2**						**6**	8
Skeiky; Yasir A. W.				**2**						**6**	8
Dillon; Davin C.				**2**						**3**	5
Gennaro; Maria Laura								**2**		**3**	5
Sadoff; Jerald C.									**2**	**3**	5
Andersen; Peter							**2**			**2**	4
Content; Jean	**2**			**2**							4
De Bruyn; Jacqueline	**2**			**2**							4
De Wit; Lucas	**2**			**2**							4
Jacobs, Jr.; William R.	**2**								**2**		4
Pescher; Pascale	**2**		**2**								4
Lodes; Michael J.										**4**	4
Marchal; Gilles	**2**		**2**								4
Romain; Felix	**2**		**2**								4
Hone; David Michael										**3**	3
Horwitz; Marcus A.					**3**						3
Houghton; Raymond L.										**3**	3
Jen; Shyian										**3**	3
Ovendale; Pamela										**3**	3
Riley; Lee W.		**3**									3
Twardzik; Daniel R.										**3**	3
Vedvick; Thomas S.										**3**	3
Bloom; Barry R.				**2**							2
Brosch; Roland										**2**	2
Cole; Stewart										**2**	2
Hess; Jurgen					**2**						2
James; Brian W.										**2**	2
Johnston; Stephen A.					**2**						2
Kaufmann; Stefan H. E.					**2**						2
Laal; Suman									**2**		2
Laqueyrerie; Anne			**2**								2
Marsh; Philip										**2**	2
McGuire; Michael J.					**2**						2
Reed; Steven G.										**2**	2
Sambandamurthy; Vasan									**2**		2
Schroder; Ulf						**2**					2
Skjot; RikkeLouiseVinther										**2**	2
Sun; Ronggai									**2**		2
Svenson; Stefan						**2**					2
Xu; Bai										**2**	2
Zolla-Pazner; Susan									**2**		2
Total	14	3	8	14	11	4	2	2	12	59	**129**

In the analysis of the science-technology relationship, it became clear that the inventors of this technological domain have an active scientific life. This pattern matches several criteria stating that inventor scientists tend to publish much more than non-inventor scientists, even years after obtaining the patent still a scientific activity around the patent can be observed (Van Looy et. al. 2006).

This is due to the fact that applied research activities are related to basic research activities (Carayol 2003), or in other words, patents stimulate the production of articles. It is even said that in the biotechnology sector more than 50% of the citations in patents refer to scientific publications (Jaques 2001).This behavior can be observed in the main inventors of this domain, who have a prolific scientific productivity, for instance:

- *Skeiky* (Skeiky and Sadoff 2006; Skeiky *et. al.* $2004_{a,b}$; Skeiky and Sadoff 2006; Skeiky *et. al*. 2009)
- *Horwitz* (Horwitz, Harth, Dillon and Maslesa-Galic 2000; Horwitz *et. al.* 1995; Horwitz *et. al.* 2005)
- *Kaufmann* (Kaufmann 2002; Kaufmann and McMichael2005; Kaufmann, Hussey and Lambert 2010; Kaufmann 2010; Kaufmann 2011);
- *Cole* (Cole et. al.1998; Cole 1999; Cole 2000);
- *Andersen* ($Andersen1994_{a,\ b}$; Andersen, Andersen, Sorensen and Nagai 1995; Andersen1997; Aagaard, Dietrich, Doherty and Andersen 2009)

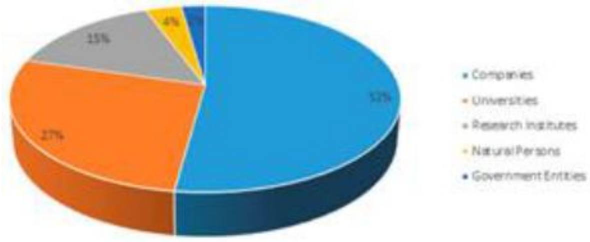
The main analyzed inventors are from United States, France, Belgium, Denmark, Germany and Canada (Map 1), in rather close correspondence with the more productive countries.



Inventores
23 Relacion(es) 1 Relacion(es) (Países)
14 Patentes 4 Patentes

Map1:Patents of Inventors by countries (more than 3 patents of the inventor by country)
Source: proINTEC

The assignees spectrum in this domain has a heterogeneous composition. The biggest percent of assignees is formed by companies, followed by universities which include hospitals serving as teaching units; then the research institutes and foundations and societies supporting the research. And with a minimal share, natural persons and government entities (Graph1).



Graph 1: Assignees spectrum

This analysis shows that TB Vaccines is a sector of science developed exclusively by researchers and academics who need infrastructure and resources to develop their work, that is why their potential is located in companies with resources, universities who hold knowledge and institutes where both requisites are fulfilled.

The main assignees of the inventions recorded about TB Vaccines are the Institut Pasteur from France located in Paris, and the Corixa Corporation from United States located in Seattle, with 13 and 14 patents respectively.

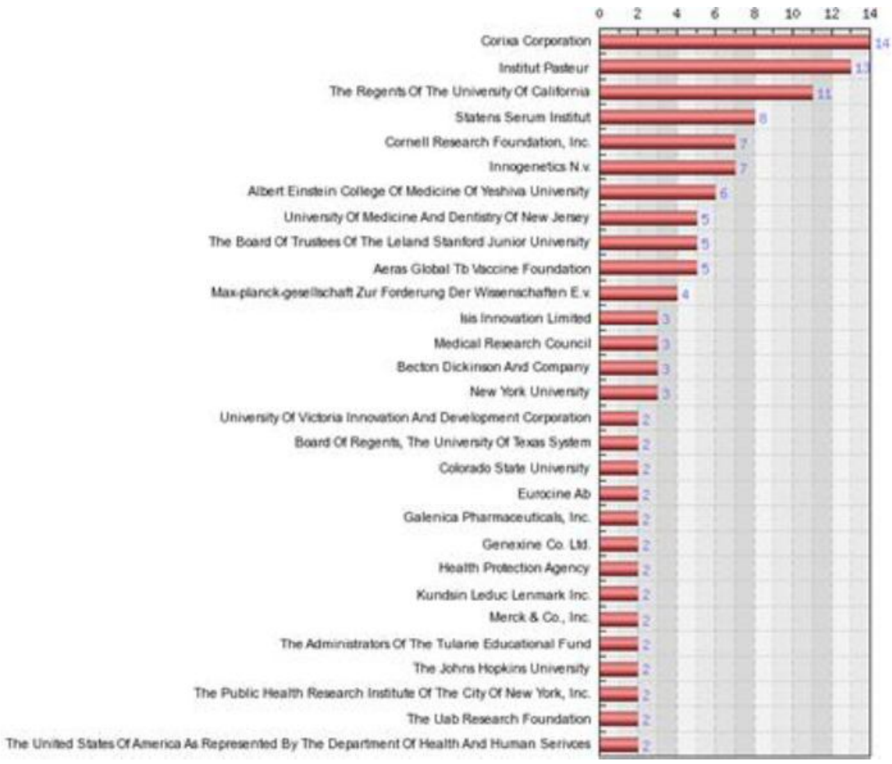
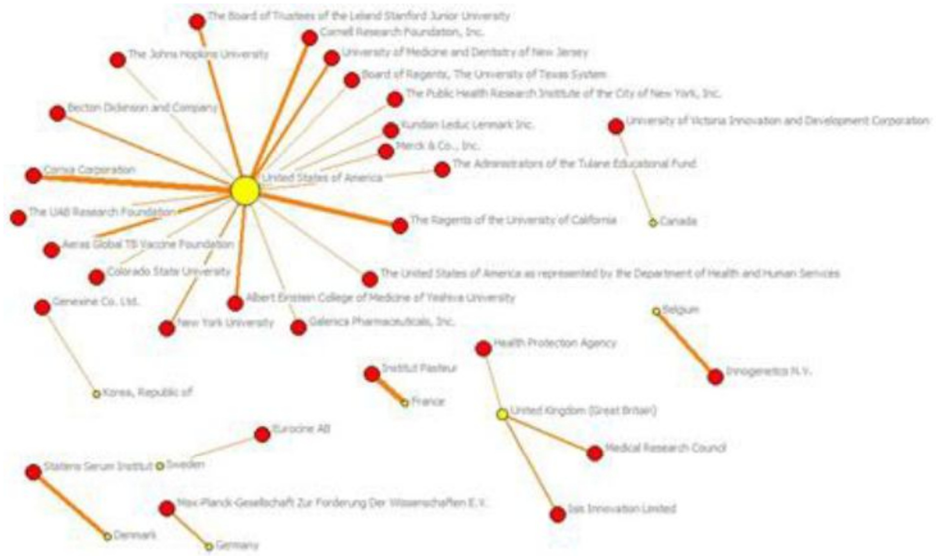


Fig.5: Amount of patents by assignee (with more than 1 patent)
Source: proINTEC

There are also other assignees with technological productivity about TB Vaccines: *The Regents of the University of California (United States), Statens Serum Institut (Denmark), Cornell Research Foundation,* *Inc. (United States), N.V. Innogenetics S.A. (Belgium), Albert Einstein College of Medicine of Yeshiva University (United States), Aeras Global TB Vaccine Foundation (United States), The Board of Trustees of the Leland Stanford Junior University (United States) and University of Medicine and Dentistry of New Jersey (United States)*(Fig. 5).

In Map 2 the fact is highlighted that most of the most productive assignees belong to the United States. Besides representing the most productive assignees from the leading countries in the subject, the map shows the most productive assignee of Denmark, Belgium, Germany, Canada, Switzerland and Korea (Map 2). These countries are emerging nowadays with patentable researches about Vaccines in the last years.



Titulares
19 Relacion(es) 1 Relacion(es) (Países).
14 Ocurrencia(s) 2 Ocurrencia(s)

Map 2:Patents by assignees by countries (more than 1 patent by assignee by country)
Source: proINTEC

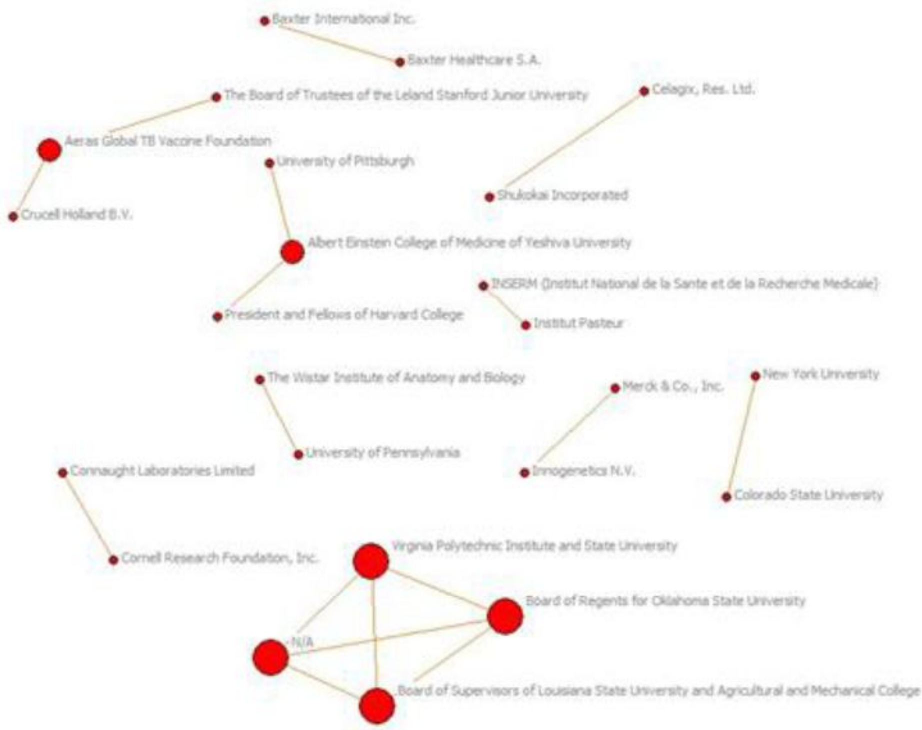
Joint relationships among assignees and inventors in the domain of TB Vaccines

A group of assignees have worked jointly in this domain to generate technologies related to TB Vaccines (Map 3). The most noticeable relationships among them are for instance: Virginia Polytechnic Institute and State University, Board of Supervisors of Louisiana State University and Agricultural and Mechanical College, and Board of Regents for Oklahoma State University, they are all assignees from the United States.

The main research relationships are established in a bigger percent with academic research centers.

CorixaCorporation is the biggest producer but it does not have joint collaboration relationships with any other research center(Map 3).

The Institut Pasteur from France has done joint research with another institute.

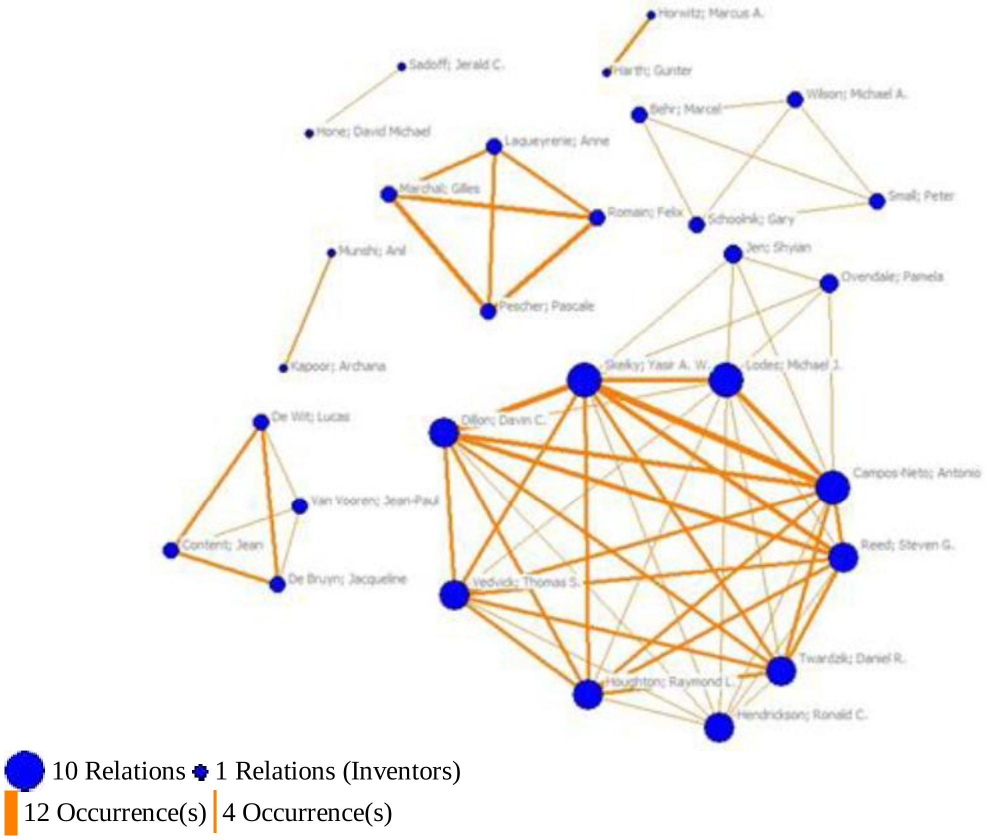


3 Relations 1 Relations (Holders)

1 Occurrence(s) 1 Occurrence(s)

Map 3: Joint Assignees in the domain TB Vaccines
Source: proINTEC

The relationships between research centers, institutes and academies, generate relationships between their researchers. There is a wide group of inventors in this domain who have worked jointly in the development of patents. The collaborators in the TB Vaccines domain, who mostly correspond to the most technologically productive of the domain, are presented in Map 4.



Map 4: Joint inventors of the domain TB Vaccines (more than 3 patents)
Source: proINTEC

The most intense collaboration link is established between the two more productive inventors of the domain, Antonio Campos Neto and Yasir A.W. Skeiky. It is followed in intensity by the relationship with other researchers like David Dillon. This could indicate that they belong to the same research team, because they all belong to United States and the Corixa Corporation.

Subject productivity: international patent classification (IPC)

This domain is comprised by 4 areas of the IPC. The biggest number of technological innovations belong to the area COMMON LIFE NEEDS (A), followed by CHEMISTRY AND METALURGICS (C), PHYSICS (G) and DIVERSE INDUSTRY TECHNIQUES – TRANSPORTS (B) (Fig. 6).

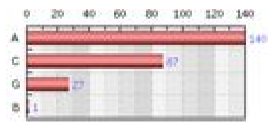
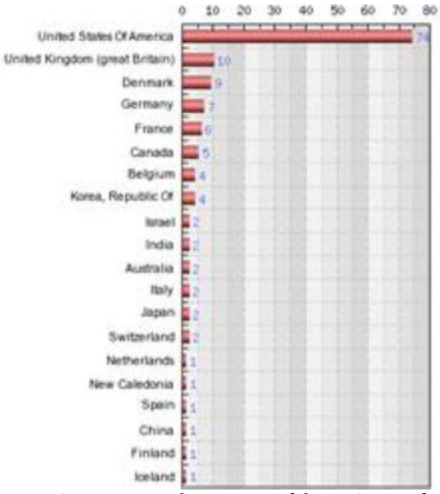


Fig. 6: Patents by IPC sections
Source: proINTEC

<u>*Section A*</u>

When each classification is analyzed separately, there are 20 countries working in section A, which correspond relatively to the productivity by countries (Fig. 7). While France is the second country with highest number of patents of the domain, it is in the fifth position in this section (Fig. 7). This could mean that their researches in this subject are mostly oriented towards other uses and applications and diagnostic techniques.



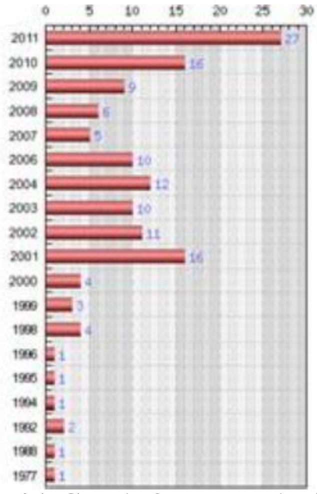
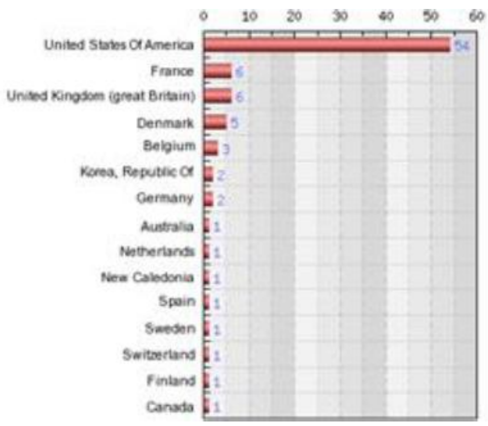


Fig. 7: Patents by country of the assignee of section A (IPC) *Fig. 8: Patents section A by year*
Source: proINTEC

- rich representation and increase of section A, appearing since 2001 with 16 patents, reaching 27 patents in 2011 (Fig.8)
- the predominance of section A might be because it groups patents related mostly with liposomes and other forms of long lasting release, key technologies for the elaboration of vaccine compounds

<u>Section C</u>

15 countries have patented technological results related to CHEMISTRY, with patents classified under section C, less than in section A(Fig. 9). France goes to the second place in researches related to section C, and Korea goes to the sixth place.



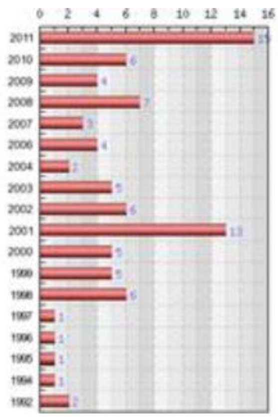


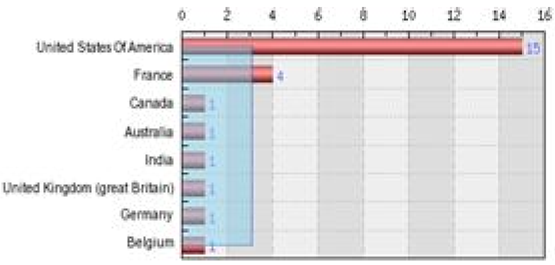
Fig. 9: Patents by country of the assignee of section C (IPC) *Fig. 10: Patent section C(IPC) by years*
Source: proINTEC

- the analysis by year shows systematic work in this subject, with 2011 as the year with the highest number of results related to Chemistry (Fig. 10)
- this behavior might be because Section C groups patents related to nucleic acids, genetic engineering techniques including genetic manipulation, creation of recombinant strands, work with plasmid vectors and bacteriophages, peptides, viruses and vectors, technologies that have been developed in the world to perform prophylactic control.

Section G

Only 8 countries are researching in the PHYSICS (G) section (Fig. 11). In this area the United Kingdom moves to the sixth place in amount of patents, with countries like Canada, Australia and India among the first positions. A remarkable fact is that one of the two patents granted to India in the USPTO, is related to Physics, holding the G classification.

- in general only emerging countries are working in this classification inside this domain
- it is shown that patents on TB Vaccines related to Physics start appearing in 1998, linking to this classification since then in almost all the years investigated
- section G groups patents mainly about immunology methods or trials and trials for microorganism studies; and about support for the immobilization of immunology compounds, which are all technological strategies widely used today in the creation of vaccines



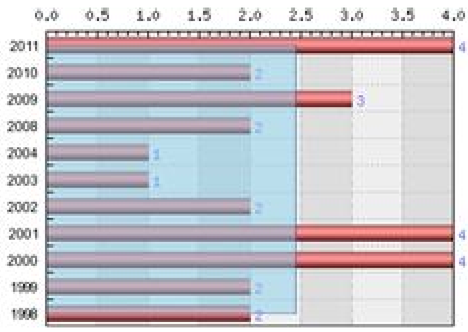


Fig. 11: Patents by country of the assignee in section G (IPC) *Fig. 12: Patents by year in section G (IPC)*

Source: proINTEC

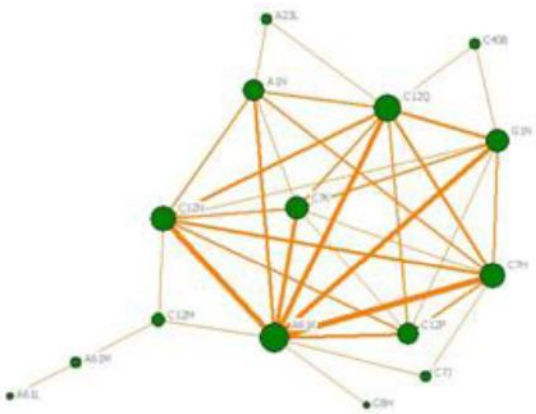
Section B

And lastly, only one patent is related to section DIVERSE INDUSTRY TECHNIQUES – TRANSPORTS (B). It was granted to France in the year 2002, being the only country having researched in this subject area inside the TB Vaccines domain.

Section B groups patents related mainly to packaging, presentation forms, filling and emptying. An example of this is the patent with this classification in this study. It is related to a device, a dispenser and spreading method for mucosal vaccines.

Joint classifications

The joint classifications established in this domain reveal the relationships between the different areas of techniques to generate new patentable technologies. In this case there are noticeable relationships between sections A and C, and also some links with specific areas inside this sections with a subject area of section G (Map 5).



10 Relations 1 Relations (CIP)
25 Occurrence(s) 1 Occurrence(s)

Map 5: Joint subclasses (IPC) of the domain TB Vaccines
Source: proINTEC

This analysis proves that in this domain there are some technological associations between classifications of sections A and C to obtain possible candidate vaccines; there are also patents using specific knowledge from one field of Physics (G1N) to generate inventions about TB Vaccines.

Citations to Patents

Patents from Corixa Corporation from United States are the most cited ones, as proven by the analysis of citations by assignee. The next in amount of citations are the patents from Statens Serum Institut from Denmark, then the inventions from The Regents of the University of California (United States), and the findings of the Albert Einstein College of Medicine of YeshivaUniversity (United States) among the most cited assignees(Fig.13).

However, the most outstanding result was to find among the most cited ones, some assignees who are not among the first places according to their productivity. In this case there are for instance: Galenica Pharmaceuticals, Inc. (United States), The Johns Hopkins University (United States) and The Public Health Research Institute of the City of New York, Inc. (United States)(Fig.13).

This behavior indicates that the claims of patents from these assignees have constituted significant outcome to generate other technologies, and even when they are not among the most productive assignees in the USPTO, their patents have become technological precedents of high relevance in the TB Vaccines domain.

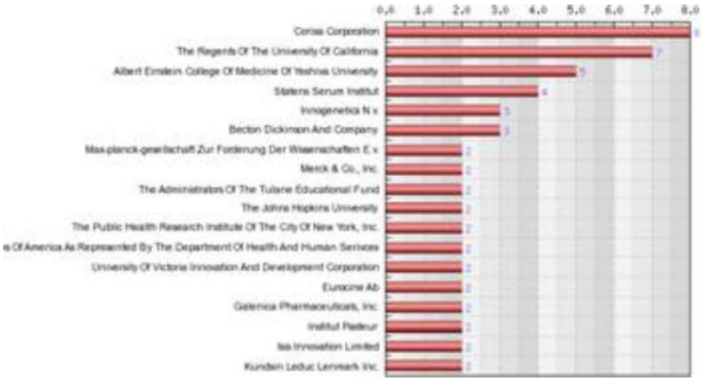


Fig.13: Amount of citations by assignee of the patent (more than 1 cite).
Source: proINTEC

A numerous representation of universities can be seen among the assignees in the citation analysis. This evidences the relevance of the Academy in the development of scientific researches, and an adequate flow of scientific-technological information between the main assignees in the research front of TB Vaccines. The citation indicator is one of the relatively more reliable measures to assess the value of patents (Díaz-Pérez and Moya-Anegón 2008). In this case it is shown that the main assignees working in the subject in the world, are those who receive more citations; their patents are assessed through citation as an important research start inside the TB Vaccines domain.

Conclusions

The work methodology being used, which included the possibility to use the international patent classification as another analysis and measurement unit for technological domains, allowed to diagnose the composition of the technical status of the case study. Some significant aspects of the technical status of the Tuberculosis Vaccines domain in the next listing evidence it:

- the productivity maximums in patents about TB Vaccines correspond to the main scientific facts published about the subject
- the geographical projection of the domain is centered and more technologically covered in highly developed countries, not in countries with the highest numbers of infections and deaths because of TB

- the countries with emerging patentable researches about TB Vaccines are Denmark, Belgium, Germany, Canada, Switzerland and Korea
- the most productive researchers in prophylactic alternatives against TB come mainly from United States, France, Belgium, Denmark, Germany and Canada
- a strong link between the basic science and the technological innovation exists in this domain, originated in the flow of scientific-technological knowledge of its inventors
- the assignees spectrum is composed mostly by companies (51.49%); followed by universities (26,97%) including hospitals and docent units; research institutes (14.61%) including also foundations and societies supporting research institutes; with a minimal share for natural persons (3.37%) and government entities (2.25%)
- most of the collaboration is established with assignees from United States. The main research relationships are established with research and academic centers
- the most cited assignees are the universities, showing an apparent flow of scientific-technological information between the main assignees. These patents become an important research entry in the domain through citation.

The classification analysis allowed to identify the technological specialization of the domain, splitting its composition by subject areas. Each subject corresponded to topics of the different technological strategies being used in the world to develop candidate vaccines against TB.

The IPC analysis shows that classification studies ease the representation of the underlying science in patent documents. It also allows to define the subject specialization by countries and years, the IPC being an essential and strategic indicator in the subject analysis of technological domains.

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Case Study of the Technical Status of a Technological Domain

Highlights

- There is evidence that from the apparition of TB also in rich countries, more funding becameavailable, leading to important discoveries which have given a push to patents grants.
- The productivity peaks in TB Vaccines patents correspond to the main milestones in this field,e.g. in 1991 with the "New use of BCGfor recombinant vaccines" (Albert Einstein College) and "Humoral and cell-mediated immune responses to olive recombinant BCG-HIV vaccine" (Withehead); in 1998 with the discovery of the mycobacteria-Tuberculosis genome; and in 2001 with "Reverse vaccinology, a genome-based approach to vaccine develoment" (Rappouli), etc.
- The geographic projection of these research projects have as its centre and largest coveragethe US, France and UK. It is shown that the technological productivity in terms of patents by country does not correspond with the countries with the highest mortality and spread of TB. Indeed, there are only 21 countries in the USPTO with holderships on alternative or improved vaccines still under design, despite the high risk humanity is suffering from TB.
- Another contribution by the research is to identify Denmark, Belgium, Germany, Canada,Korea and Switzerland as countries where currently new patentable vaccines are being developed, which can climb up to higher position in the field if they maintain their level of innovation activity in the next years.
- Amongst the most productive researchers working on prophylactic alternatives we noteAntonio Campos-Neto, YasirSkeiky, Peter Andersen, Laura MaríaGennaro, Jerald C. Sadoff, Davin C. Dillon, Lucas De Wit, etc. They come mostly from US, France, Belgium, Denmark, Germany and Canada, which corresponds relatively well with the productivity by country.
- The study allowed to ascertain in addition that the most important inventors are working on asustained effort along with an adequate patenting policy. It was shown that the inventors in this scientific discipline have an active scientific curriculum and that there is a close link in between basic sciences and technological innovation in the field of TB Vaccines.
- The most important holders of registered inventions on TB Vaccines are the Institut Pasteurof Francia and the Corixa Corporation of the US. Also listed with the most productive holders are : The Regents of the University of California (US), Statens Serum Institut (Denmark), Cornell Research Foundation Inc. (US), N.V. InnogeneticsS.A. (Belgium), Albert Einstein College of Medicine of Yeshiva University (US), Aeras Global TB Vaccine Foundation (US), The Board of Trustees of the Leland Stanford Junior University (US) and the University of Medicine and Dentistry of New Jersey (US).
- The strongest co-operation links exist within US patent holders, and the strongest researchlinks exist with research centers and academics.
- The TB Vaccines patents relate to 4 thematic areas. This shows that such researchnecessitates a wide scientific and technological base in order to develop patents; the raise of the Physics sector brings the most significant new impulse in the emerging TB Vaccines technology.
- The patents of the Corixa Corporation are the most cited ones, followed by the patents of theStatens Serum Institut of Denmark, the inventions of The Regents of the University of California, and the discoveries of the Albert Einstein College of Medicine of Yeshiva University.

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