Innovation Status of Gene Therapy for Breast Cancer

Maricruz Anaya-Ruiz1, Martin Perez-Santos2*

Abstract

Background: To analyze multi-source data including publications and patents, and try to draw the whole landscape of the research and development community in the field of gene therapy for breast cancer. Materials and Methods: Publications and patents were collected from the Web of science and databases of the five major patent offices of the world, respectively. Bibliometric methodologies and technology are used to investigate publications/patents, their contents and relationships. Results: A total of 2,043 items published and 947 patents from 1994 to 2013 including “gene therapy for breast cancer” were retrieved. The top five countries in global publication share were USA, China, Germany, Japan and England. On the other hand, USA, Australia, England, South Korea and Japan were the main producers of patents. The universities and enterprises of USA had the highest amount of publication and patents. Adenovirus- and retrovirus-based gene therapies and small interfering RNA (siRNA) interference therapies were the main topics both in publications and patents. Conclusions: The above results show that global research in the field of gene therapy for breast cancer is increasing and the main participants in this field are USA and Canada in North America, China, Japan and South Korea in Asia, and England, Germany, and Italy in Europe. Also, this article demonstrates the usefulness of bibliometrics to address key evaluation questions and define future areas of research.

Keywords: Breast cancer - gene therapy - patents - publications - innovation

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Introduction

Breast cancer remains a major public health problem. Currently, among all cancers, breast cancer is the most common cancer in women in both developed and developing countries (Anaya-Ruiz et al., 2014; Dogan and Toprak, 2014; Shi et al., 2014; Malvezzi et al., 2014; Youlden et al., 2014). According to GLOBOCAN estimates, more than half (52.9%) of 1.67 million new breast cancer cases were diagnosed in developing countries in 2012 (Ferlay et al., 2014).

The treatment of breast cancer has improved over recent years and has led to an increased survival rate for patients. Current clinical therapies for breast cancer are offered on an individual patient basis via a multidisciplinary team and comprise surgery, radiotherapy and drug therapies targeting oncogenic processes (Majeed et al., 2014). However, in recent years gene therapy has emerged as a viable treatment option, yet actually there are still no approved gene therapy products for breast cancer (McCrudden and McCarthy, 2014). Gene therapy is a new treatment modality in which new gene is introduced or existing gene is manipulated to cause cancer cell death or slow the growth of the tumor. There are different approaches: gene addition therapy, viral gene therapy, nonviral gene therapy, and RNA interference-based gene therapy (Ibraheem et al., 2014; Petrocca and Lieberman, 2014; Walther and Schlag, 2014).

Furthermore, extensive research has been conducted to solve the problem of breast cancer, but the remedy still remains uncertain. Faced with this dilemma, scientific research evaluation has as purpose monitoring of ongoing research initiatives to assess the efficiency and effectiveness with which they are being implemented, and to determine the extent to which they are achieving their targeted objectives, and to recommend adjustments. On this premise, the present study was designed to determine the world share of publications and patents, in the field of gene therapy for breast cancer from 1994 to 2013.

Materials and Methods

We used a keyword search approach to identify the "gene therapy for breast cancer"-related publications and patents data from Web of Science and patent’s databases from United State Patent and Trademark Office, European Patent Office, State Intellectual Property Office of the People Republic of China, Japan Patent Office, Korean Intellectual Property Office and World Intellectual Property Office. In this study, Web of Science, which covering nearly all fields of science, was used to produce statistics on the scientific production of gene therapy for breast cancer. Gene therapy articles and reviews, in the field of breast cancer, were downloaded for the 20
publication years, 1994-2013. In order to approximate the overall number of items on breast cancer, the following search strategy was employed; TS= [(gene therap*) OR (DNA therap*)] AND TS=[(breast invasive ductal carcinoma) OR (infiltrating duct carcinoma$) OR (mammary ductal carcinoma$) OR (breast cancer) OR (breast neoplasm$) OR (breast tumo$r$) OR (human mammary neoplasm$) OR (human mammary carcinoma$)]; where TS= Topic search, $=any character, *=two or more character. The same search strategic was performed in the Title/Abstract/Claims of the patent document.

Document information included numbers of years of publication, citations, origin countries, source journals, institutes and enterprises, and publication/patent topics. The records were downloaded using Microsoft Excel software, and additional coding was manually performed for the above fields.

Results

A total of 2043 items published and 947 patent documents from 1994 to 2013 including "gene therapy for breast cancer" were counted (Figure 1). A development trend was found for items published, which increased from 22 in 1994 to 148 publications in 2013. However, the development trend of patents had publication's different behavior as a growth trend was observed to peak in 2004 (98), then initiating a decrease thereof to stabilize in the period 2009-2013 (27 on average each year).

The global publication share of top 15 most productive countries in gene therapy for breast cancer is shown in Table 1, with USA occupying the first rank and contributing the largest publication share (48.02%), followed by China (16.25%, 2nd rank), Germany (7.73%, 3rd rank), Japan (7.05%, 4th rank), England (5.8%, 5th rank), Canada, Italy, France, South Korea and Finland (from 5.24% to 1.91% publication share and rank from 6th to 10th), Netherlands, Switzerland, Finland, Australia and Sweden (from 1.42% to 1.13% publication share and rank from 11th to 15th). The global publication share has witnessed the largest increase of 31.69% in China, followed by South Korea (3.69%), Spain (1.6%), Netherlands (1.55%), Finland (1.1%),

Table 1. Global Publication Output, and Share (Parenthetical) of Top 15 Most Productive Countries in “Gene Therapy for Breast Cancer”, 1994-2013

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>United States of America</td>
<td>133 (59.91)</td>
<td>309 (57.01)</td>
<td>281 (49.38)</td>
<td>258 (36.34)</td>
<td>981 (48.02)</td>
</tr>
<tr>
<td>People Republic China</td>
<td>0</td>
<td>19 (3.5)</td>
<td>88 (15.47)</td>
<td>225 (31.69)</td>
<td>332 (16.25)</td>
</tr>
<tr>
<td>Germany</td>
<td>21 (9.46)</td>
<td>42 (7.75)</td>
<td>45 (7.91)</td>
<td>50 (7.04)</td>
<td>158 (7.73)</td>
</tr>
<tr>
<td>Japan</td>
<td>10 (4.5)</td>
<td>50 (9.22)</td>
<td>47 (8.26)</td>
<td>37 (5.21)</td>
<td>144 (7.05)</td>
</tr>
<tr>
<td>England</td>
<td>8 (3.6)</td>
<td>44 (8.12)</td>
<td>34 (5.97)</td>
<td>28 (3.94)</td>
<td>114 (5.58)</td>
</tr>
<tr>
<td>Canada</td>
<td>20 (9)</td>
<td>36 (6.64)</td>
<td>19 (3.34)</td>
<td>32 (4.51)</td>
<td>107 (5.24)</td>
</tr>
<tr>
<td>Italy</td>
<td>17 (7.66)</td>
<td>29 (5.35)</td>
<td>22 (3.86)</td>
<td>22 (3.1)</td>
<td>90 (4.4)</td>
</tr>
<tr>
<td>France</td>
<td>8 (3.6)</td>
<td>28 (5.16)</td>
<td>29 (5.1)</td>
<td>16 (2.25)</td>
<td>81 (3.96)</td>
</tr>
<tr>
<td>South Korea</td>
<td>4 (1.8)</td>
<td>11 (2.03)</td>
<td>22 (3.87)</td>
<td>39 (5.49)</td>
<td>76 (3.72)</td>
</tr>
<tr>
<td>Spain</td>
<td>2 (0.9)</td>
<td>10 (1.84)</td>
<td>9 (1.58)</td>
<td>18 (2.53)</td>
<td>39 (1.91)</td>
</tr>
<tr>
<td>Netherlands</td>
<td>0</td>
<td>10 (1.84)</td>
<td>7 (1.23)</td>
<td>11 (1.55)</td>
<td>29 (1.42)</td>
</tr>
<tr>
<td>Switzerland</td>
<td>7 (3.15)</td>
<td>10 (1.84)</td>
<td>3 (0.53)</td>
<td>5 (0.7)</td>
<td>25 (1.22)</td>
</tr>
<tr>
<td>Finland</td>
<td>1 (0.45)</td>
<td>3 (0.55)</td>
<td>10 (1.78)</td>
<td>11 (1.55)</td>
<td>25 (1.22)</td>
</tr>
<tr>
<td>Australia</td>
<td>2 (0.9)</td>
<td>3 (0.55)</td>
<td>5 (0.88)</td>
<td>14 (1.97)</td>
<td>24 (1.17)</td>
</tr>
<tr>
<td>Sweden</td>
<td>2 (0.9)</td>
<td>6 (1.11)</td>
<td>6 (1.05)</td>
<td>9 (1.27)</td>
<td>23 (1.13)</td>
</tr>
</tbody>
</table>

Table 2. Total Papers, Citations, Average Citation Impact Per Paper and High Cited Papers of 15 Most Productive Countries in “Gene Therapy for Breast Cancer”, 1994-2013

<table>
<thead>
<tr>
<th>Country</th>
<th>TP</th>
<th>TC</th>
<th>SC</th>
<th>ACPP</th>
<th>HCP</th>
</tr>
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<tbody>
<tr>
<td>United States of America</td>
<td>981</td>
<td>33992</td>
<td>59.08</td>
<td>34.65</td>
<td>72</td>
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<tr>
<td>People Republic China</td>
<td>332</td>
<td>3441</td>
<td>5.98</td>
<td>10.64</td>
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<tr>
<td>Germany</td>
<td>158</td>
<td>4153</td>
<td>7.22</td>
<td>26.28</td>
<td>6</td>
</tr>
<tr>
<td>Japan</td>
<td>144</td>
<td>3337</td>
<td>5.8</td>
<td>23.17</td>
<td>2</td>
</tr>
<tr>
<td>England</td>
<td>114</td>
<td>4992</td>
<td>8.68</td>
<td>43.79</td>
<td>13</td>
</tr>
<tr>
<td>Canada</td>
<td>107</td>
<td>3864</td>
<td>6.72</td>
<td>31.11</td>
<td>12</td>
</tr>
<tr>
<td>Italy</td>
<td>90</td>
<td>2320</td>
<td>4.03</td>
<td>25.78</td>
<td>4</td>
</tr>
<tr>
<td>France</td>
<td>81</td>
<td>2523</td>
<td>4.38</td>
<td>31.15</td>
<td>7</td>
</tr>
<tr>
<td>South Korea</td>
<td>76</td>
<td>1212</td>
<td>2.11</td>
<td>15.95</td>
<td>1</td>
</tr>
<tr>
<td>Spain</td>
<td>39</td>
<td>692</td>
<td>1.2</td>
<td>17.74</td>
<td>0</td>
</tr>
<tr>
<td>Netherlands</td>
<td>29</td>
<td>1230</td>
<td>2.14</td>
<td>42.41</td>
<td>3</td>
</tr>
<tr>
<td>Switzerland</td>
<td>25</td>
<td>1231</td>
<td>2.14</td>
<td>49.24</td>
<td>5</td>
</tr>
<tr>
<td>Finland</td>
<td>25</td>
<td>667</td>
<td>1.16</td>
<td>26.68</td>
<td>2</td>
</tr>
<tr>
<td>Australia</td>
<td>24</td>
<td>777</td>
<td>1.35</td>
<td>32.36</td>
<td>1</td>
</tr>
<tr>
<td>Sweden</td>
<td>23</td>
<td>752</td>
<td>1.3</td>
<td>32.7</td>
<td>1</td>
</tr>
</tbody>
</table>

*TP: Total papers; TC: Total citations; SC: Share citations; ACPP: Average citation per paper; HCP: High cited papers

Table 3. Top Journals Publishing Articles in the Field of “Gene Therapy For Breast Cancer”, 1994-2013

<table>
<thead>
<tr>
<th>Journal</th>
<th>Papers</th>
<th>% 5-year impact factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer Gene Therapy</td>
<td>208</td>
<td>10.18 2.637</td>
</tr>
<tr>
<td>Gene Therapy</td>
<td>101</td>
<td>4.94   3.67</td>
</tr>
<tr>
<td>Cancer Research</td>
<td>75</td>
<td>3.67   8.958</td>
</tr>
<tr>
<td>Human Gene Therapy</td>
<td>72</td>
<td>3.52   3.435</td>
</tr>
<tr>
<td>Clinical Cancer Research</td>
<td>42</td>
<td>2.05   8.101</td>
</tr>
<tr>
<td>Molecular Therapy</td>
<td>41</td>
<td>2      6.351</td>
</tr>
<tr>
<td>Molecular Cancer Therapeutics</td>
<td>31</td>
<td>1.52  5.858</td>
</tr>
<tr>
<td>Journal of Gene Medicine</td>
<td>31</td>
<td>1.52   2.109</td>
</tr>
<tr>
<td>Oncogene</td>
<td>29</td>
<td>1.42   7.719</td>
</tr>
<tr>
<td>Oncology Reports</td>
<td>27</td>
<td>1.32   2.121</td>
</tr>
<tr>
<td>International Journal of Oncology</td>
<td>25</td>
<td>1.22   2.741</td>
</tr>
<tr>
<td>Cancer Letters</td>
<td>25</td>
<td>1.22   4.879</td>
</tr>
<tr>
<td>Breast Cancer Research and Treatment</td>
<td>22</td>
<td>1.07  4.274</td>
</tr>
<tr>
<td>International Journal of Cancer</td>
<td>21</td>
<td>1.03   5.497</td>
</tr>
<tr>
<td>Anticancer Research</td>
<td>21</td>
<td>1.03   1.879</td>
</tr>
</tbody>
</table>
Breast cancer is an emerging public health problem globally. Breast cancer research evaluation allows...
answering questions related to the performance of research to determine the extent to which they are achieving their targeted objectives, and to recommend adjustments.

This study analyzed publications and patents in the field of gene therapy for breast cancer and some important points about the trend of research in this field were obtained. Our findings suggest a growing interest in the field of gene therapy for breast cancer as shown by the increased number of items each year.

This analysis has also demonstrated the leading role which the United States plays in gene therapy for breast cancer research, due to the following: a) it is the largest producer of scientific papers, b) is the leading producer of patents, c) has eleven of the fifteen major institutions/ companies producing scientific articles, and d) has nine of the top ten institutions/production companies of patents in the field of gene therapy for breast cancer. The present study shows predominance in research and patents for the following countries: USA and Canada in America, China, Japan and South Korea in Asia, and England, Germany, and Italy in Europe.

Other different studies have examined several fields in breast cancer research. For example, the trends for breast cancer research have been addressed in several countries such as Mexico (Perez-Santos and Anaya-Ruiz, 2013), Iran (Shahkhodabandeh et al., 2009), Portugal (Donato and De Oliveira, 2006), and China (Hong and Dong, 2014). On the other hand, there is another study in the field of breast cancer diet, which shows that the main participating countries are consistent with fifteen of the present study (Kotepui et al., 2014). Additionally, a study of reconstructive breast surgery research shows a match between the same countries group obtained in our study (Moghimi et al., 2013). Similarly, Ha et al. (2014) shows that USA is the leader in articles published in the field of breast cancer imaging research. Regarding patent data in the field of gene therapy for breast cancer, it is inexplicable that the trend had a peak in 2004 and then begins to decline. Consistent with these findings, the results obtained by Antunes et al. show that patents for breast cancer has a peak in 2004-2005 and then begin to decline in the activity of claiming patents (Antunes et al., 2013).

There are few studies based on data integration of research publications and patents, or any two of them. This work represents the first bibliometric assessment of gene therapy for breast cancer research that includes publications and patents. The findings of this study should provide useful information for those who will be performing research and studying gene therapy for breast cancer and for prospective models in the study of breast cancer (Canongia, 2007).

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References


