



Review

Bibliometric analysis of global research on PD-1 and PD-L1 in the field of cancer

Ya Gao^{a,b}, Shuzhen Shi^{a,b}, Wenjuan Ma^{a,b}, Ji Chen^c, Yitong Cai^c, Long Ge^{a,b,d}, Lun Li^e, Jiarui Wu^f,
Jinhui Tian^{a,b,*}

^a Evidence-Based Medicine Center, School of Basic Medical Sciences, Lanzhou University, Lanzhou, China

^b Key Laboratory of Evidence-Based Medicine and Knowledge Translation of Gansu Province, Lanzhou, China

^c Evidence-Based Nursery Center, School of Nursing, Lanzhou University, Lanzhou, China

^d School of Public Health, Lanzhou University, Lanzhou, China

^e Shanghai Cancer Center of Fudan University, Shanghai, China

^f Department of Clinical Chinese Pharmacy, School of Chinese Materia Medica, Beijing University of Chinese Medicine, Beijing, China

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ABSTRACT

Objectives: To identify the cooperation of authors, countries, and institutions and explore the hot topics and future prospects regarding programmed cell death protein 1 (PD-1) and programmed cell death 1 ligand 1 (PD-L1) research.

Materials and methods: Publications on PD-1 and PD-L1 research were retrieved from the Web of Science Core Collection. Bibliometric analyses were performed using VOSviewer 1.6.9, HistCite 2.1, and CiteSpace V software. Network maps were generated to evaluate the collaborations between different authors, countries, and institutions.

Results: A total of 7359 articles related to PD-1 and PD-L1 research in the field of cancer were identified. We observed rapid growth in the number of publications since 2014. *Oncoimmunology* (326, 4.43%) had the highest number of publications, while *N Engl J Med* (18,828 co-citations, 6.30%) was the most co-cited journal. Hodi FS and Wolchok JD were key researchers. There were active collaborations among the top authors. The USA was the leading contributor in this field with 3496 publications. Active cooperations between countries and between institutions were observed. The main hot topics included matters related to the efficacy and prognosis of various tumors after treatment with PD-1 and/or PD-L1 inhibitors, as well as the activation or expression of important immunological factors targeted at tumors.

Conclusion: PD-1 and PD-L1 studies have significantly increased after 2014. The USA contributed the most publications. There were active cooperations between authors, countries, and institutions. Further research should expand and develop new topics such as those likely to boost therapeutic strategies for cancer.

1. Introduction

Cancer is the second leading cause of death in the world, with an estimated 9.6 million deaths in 2018 [1]. It is estimated that by 2035, about a quarter of the world's population will be directly affected by cancer [2]. Fortunately, due to the development of new diagnostic and therapeutic methods, cancer-related deaths have fallen by 23% over the past 20 years [3]. The main treatments for cancer include surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy [2,4]. In recent years, cancer immunotherapy has witnessed great advantages and has become the most promising treatment approach for

cancers [5,6]. It is expected to be an important part of many treatment programs and is now used to treat many types of cancers [7,8].

Programmed cell death protein 1 (PD-1) is an immune checkpoint receptor encoded by PDCD1 gene which mediates immunosuppression [9,10]. PD-1 is expressed on various cells, such as NK cells, B cells, dendritic cells, antigen presenting cells, activated CD4⁺ T cells and CD8⁺ T cells, as well as monocytes [10–12]. However, it mainly plays a role in peripheral tissues [9]. When PD-1 binds to one of its ligands, programmed cell death 1 ligand 1 (PD-L1) or PD-L2, it inhibits the activation of T cells [13]. Based on this mechanism, many immune checkpoint inhibitors have been developed for the treatment of non-

* Corresponding author at: Evidence-Based Medicine Center, School of Basic Medical Sciences, Lanzhou University, No.199, Donggang West Road, Lanzhou City 730000, Gansu Province, China.

E-mail address: tianjh@lzu.edu.cn (J. Tian).

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Table 1
The top 10 journals and co-cited journals of PD-1 and PD-L1 research in the cancer field [n (%)].

Rank	Journal	N (%)	Country	IF (2017)	Co-cited journal	Co-citation	Country	IF (2017)
1	Oncoimmunology	326 (4.43%)	USA	5.503	N Engl J Med	18,828 (6.30%)	USA	79.258
2	Oncotarget	316 (4.29%)	USA	0	J Clin Oncol	12,956 (4.33%)	USA	26.303
3	Clin Cancer Res	281 (3.82%)	USA	10.199	Clin Cancer Res	11,705 (3.91%)	USA	10.199
4	Cancer Immunol Res	180 (2.45%)	USA	9.188	J Immunol	9251 (3.09%)	USA	4.539
5	J Immunother Cancer	165 (2.24%)	UK	8.374	Cancer Res	9122 (3.05%)	USA	9.13
6	Cancer Res	162 (2.20%)	USA	9.13	Nature	8514 (2.85%)	UK	41.577
7	Plos One	153 (2.08%)	USA	2.766	Blood	6688 (2.24%)	USA	15.132
8	Cancer Immunol Immunother	117 (1.59%)	Germany	4.225	Proc Natl Acad Sci USA	6614 (2.21%)	USA	9.504
9	Sci Rep	101 (1.37%)	UK	4.122	J Exp Med	6368 (2.13%)	USA	10.79
10	Lung Cancer	95 (1.29%)	Netherlands	4.486	Science	6061 (2.03%)	USA	41.058

small-cell lung cancer [14], Hodgkin's lymphoma [15], melanomas [16,17], and renal cell carcinoma [18]. Recently, some systematic reviews have been conducted to evaluate the efficacy of PD-1 inhibitors or PD-L1 inhibitors for melanoma or non-small-cell lung cancer [19–21]. Other systematic reviews have analyzed the adverse events in patients treated with PD-1 inhibitors or PD-L1 inhibitors [22,23]. However, the status of research in the area of PD-1 and PD-L1 in the cancer field and other related topics have not been investigated.

In the present study, a bibliometric analysis was conducted to (1) determine the research landscape of PD-1 and PD-L1 in terms of the year, journals, co-cited journals, authors, countries, institutions, keywords, and references; (2) identify the cooperation among authors, countries and institutions; (3) and explore the key topics and developments.

2. Methods

2.1. Data source and search strategy

A comprehensive search was performed online using the Web of Science (WoS) Core Collection database on February 1, 2019. The search terms were Pembrolizumab, Avelumab, Atezolizumab, Nivolumab, Durvalumab, Pidilizumab, PD-1, PD-L1, B7-H1 Antigen, Neoplasm, Tumor, Cancer, and their synonyms. A detailed search strategy is presented in Supplementary 1. The time period of publication was from the inception of the database to December 31, 2018. The search was performed on a single day to avoid bias caused by the daily database updates. In the present study, only articles were included. There was no restriction on language and data category. The search retrieved 7359 studies that met the inclusion criteria.

2.2. Data analysis

HistCite 2.1 (HistCite Software LLC, New York, USA) was used to analyze the publication language, publication year, and co-cited references. VOSviewer 1.6.9 (Leiden University, Leiden, Netherlands) was used to identify journals, co-cited journals, countries, institutions, and design a network map for productive countries and institutions, which helped to visualize collaborative teams [24]. The impact factors (IF) of journals were obtained from the 2018 Journal Citation Reports (JCR) (Clarivate Analytics, Philadelphia, USA) [25]. A cluster analysis was performed and a network map together with a density map for high-frequency keywords were created using VOSviewer. In the network maps, different nodes represented elements such as country, institution, and keyword while the size of the nodes reflected the number of publications or frequency [26]. The links between nodes represented relationships such as collaboration, co-occurrence or co-citations [27,28]. The color of nodes and lines represented different clusters or years [29]. CiteSpace is a scientific software that reveals the trends and dynamics in scientific literature as well as identifies key points in a given research field [30,31]. CiteSpace was therefore used to design the social network

map for authors, the dual-map overlay for journals, and detect citation bursts for references.

The fractional counting method of VOSviewer was used and customized to ignore documents with many authors (maximum number of authors per document: 25). The parameters of CiteSpace used were as follows: time slicing (1991–2018), years per slice (1), term source (all selection), node type (choose one at a time), selection criteria (50), pruning (none), and visualization (cluster view-static, show merged network).

3. Results

3.1. Publication language

A total of 7359 articles, published in eleven languages were retrieved. Of the 7359 papers, 7178 (97.54%) were published in English, 83 (1.13%) in German, 81 (1.10%) in French, 5 (0.07%) in Polish, 5 (0.07%) in Spanish, 2 (0.03%) in Hungarian, and 1 (0.01%) in Chinese, Japanese, Korean, Portuguese, and Rumanian.

3.2. Journals and co-cited journals

Co-cited journals are those that are often cited together by other scholars. All the 7359 papers were published in 953 journals. Table 1 presented the top 10 journals and co-cited journals in PD-1 and PD-L1 field. The top 10 journals contributed 1896 (25.76%) papers. *Oncoimmunology* (326, 4.43%) ranked first, followed by *Oncotarget* (316, 4.29%), *Clin Cancer Res* (281, 3.82%), *Cancer Immunol Res* (180, 2.45%), and *J Immunother Cancer* (165, 2.24%). Among the top 10 journals, six were from the United States (USA), two from the United Kingdom (UK), one from Germany, one from the Netherlands, and the impact factors of six journals were lower than 6.000. *N Engl J Med* (18,828 co-citations, 6.30%), *J Clin Oncol* (12,956 co-citations, 4.33%), *Clin Cancer Res* (11,705 co-citations, 3.91%), *J Immunol* (9251 co-citations, 3.09%), and *Cancer Res* (9122 co-citations, 3.05%) were the top 5 co-cited journals. All the co-citations of the top 10 journals were greater than 6000. 90.00% of the top 10 co-cited journals were from the USA, 70.00% had impact factors higher than 10.000.

Fig. 1 presents the dual-map overlay of journals. The left side represents the map of citing journals and the right side represents the map of the cited journals. The label represents the subject covered by the journal [32]. Colored curves represent paths of references, where each curve originates from the citing map and points to the cited map [33]. There were four main citation paths in the current map.

3.3. Publication outputs

The first study on PD-1 and PD-L1 in the field of cancer was published in 1991, while the number of publications per year before 2003 were less than 5 (Fig. 2). Between 2003 and 2010, the number of publications slightly increased, but the annual scholarly output was still

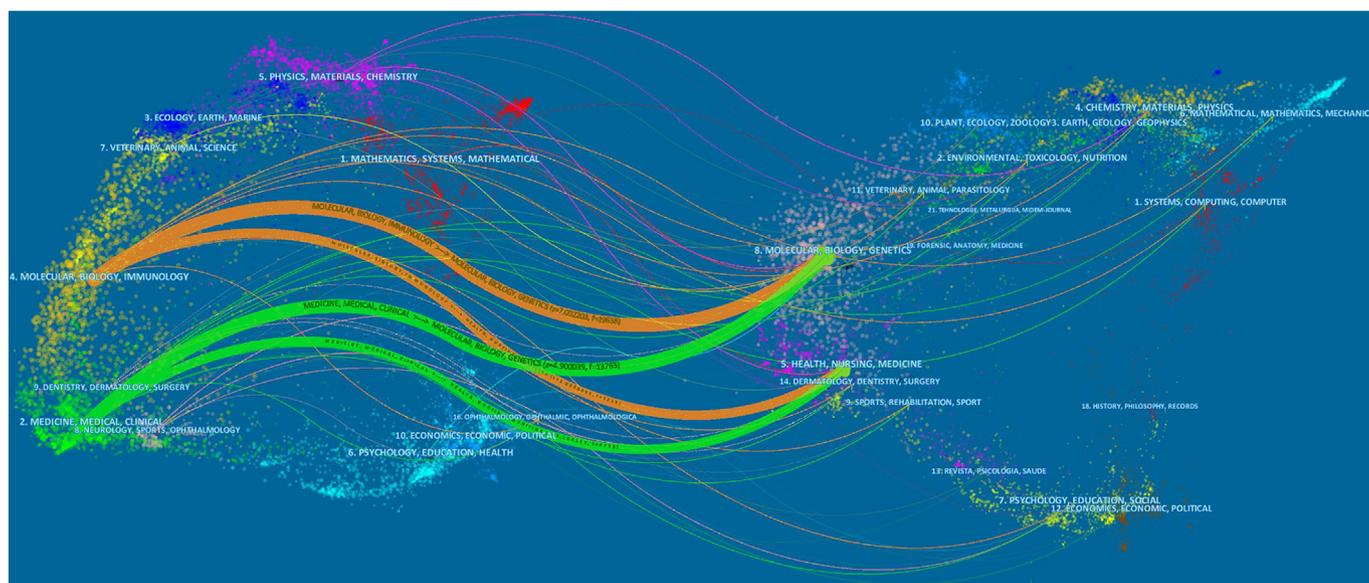


Fig. 1. The dual-map overlay of journals related to PD-1 and PD-L1 research in the cancer field. (For interpretation of the references to color in this figure, the reader is referred to the web version of this article.)

less than 100. After 2010, the number of annual publications started increasing rapidly, especially after 2014. The number of annual publications gradually increased from 101 in 2011, 289 in 2014, 558 in 2015, 1142 in 2016, 1966 in 2017, to 2705 in 2018. From 2015 to 2018, 6371 PD-1 and PD-L1 papers were published, accounting for 86.57% of all the included studies.

3.4. Authors and co-cited authors

Co-cited authors mean that the authors are cited together, and the map of authors and co-cited authors provides information about influential research groups and potential collaborators [29]. A total of 40,230 authors were obtained in the 7359 article publications. Table 2 shows the top 10 authors and co-cited authors. The top 10 authors contributed 627 (8.52%) papers. Hodi FS (91, 1.24%) published the highest number of manuscripts, followed by Freeman GJ (84, 1.14%),

Table 2

The top 10 authors and co-cited authors of PD-1 and PD-L1 research in the cancer field [n (%)].

Rank	Author	N (%)	Co-cited author	Citations
1	Hodi FS	91 (1.24%)	Topalian, SL	2919 (0.98%)
2	Freeman GJ	84 (1.14%)	Robert C	2006 (0.67%)
3	Zhang Y	74 (1.01%)	Brahmer JR	1729 (0.58%)
4	Wolchok JD	66 (0.90%)	Herbst RS	1454 (0.49%)
5	Wang Y	63 (0.86%)	Hodi FS	1425 (0.48%)
6	Wang J	55 (0.75%)	Dong HD	1371 (0.46%)
7	Zhang L	53 (0.72%)	Pardoll DM	1190 (0.40%)
8	Zhang J	47 (0.64%)	Wolchok JD	1136 (0.38%)
9	Schadendorf D	47 (0.64%)	Rizvi NA	1085 (0.36%)
10	Ribas A	47 (0.64%)	Taube JM	1026 (0.34%)

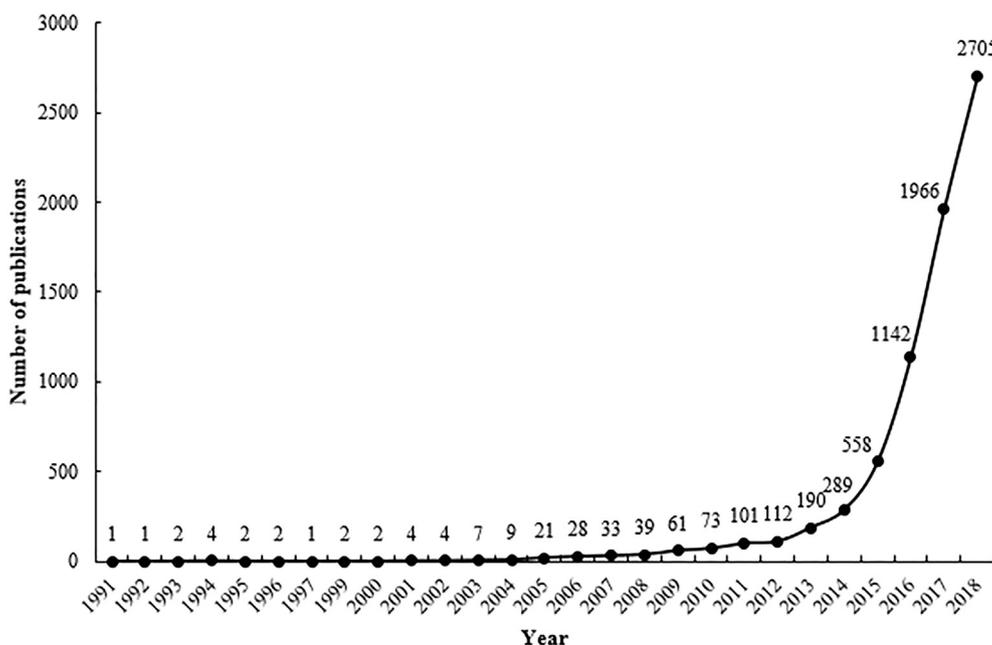


Fig. 2. Publication years of PD-1 and PD-L1 research in the cancer field.

Timespan: 1991-2018 (Slice Length=1)
 Selection Criteria: Top 50 per slice, LRF=2, LBY=8, e=2.0
 Network: N=476, E=1309 (Density=0.0116)
 Largest CC: 299 (62%)
 Nodes Labeled: 5.0%
 Pruning: None

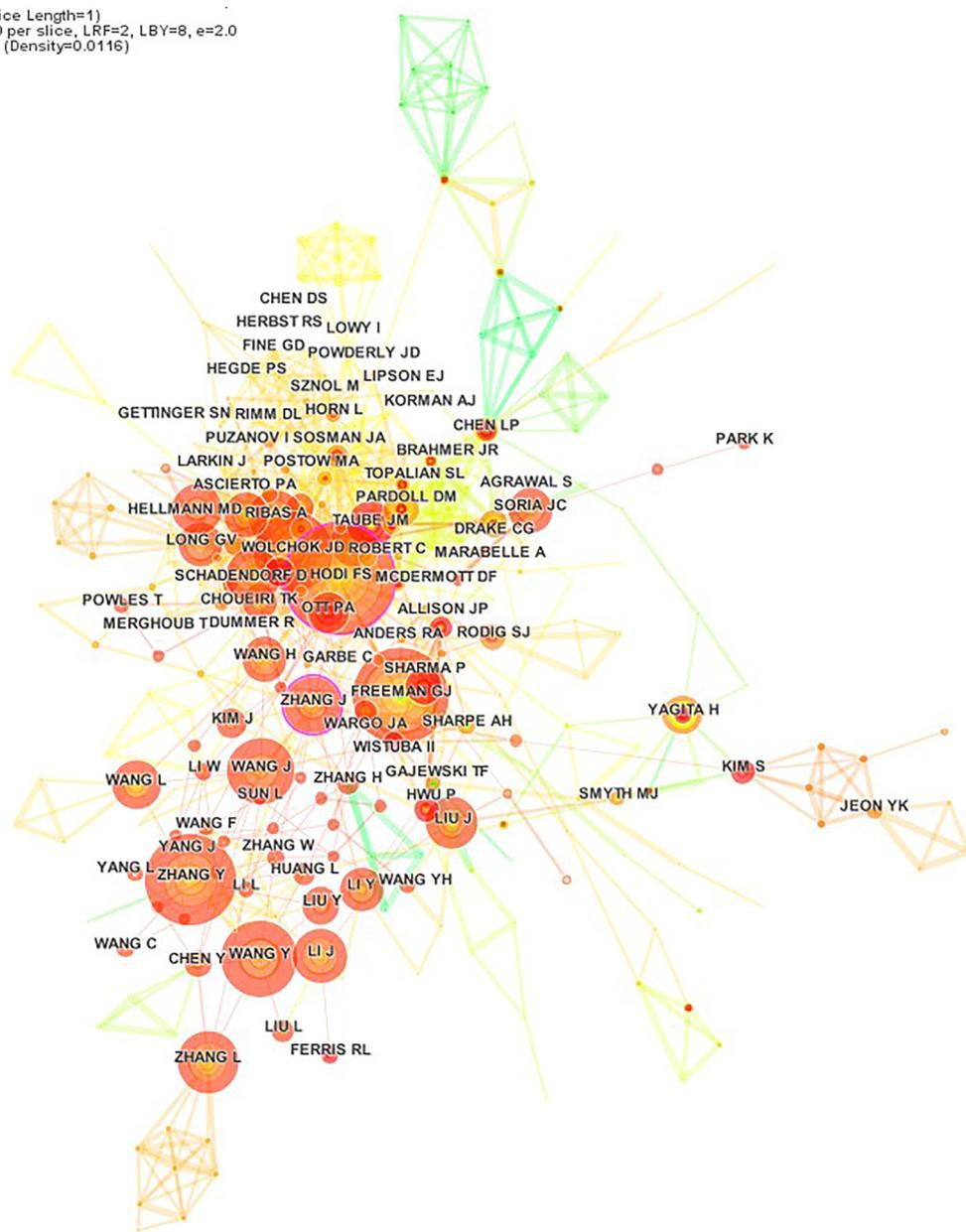


Fig. 3. The network map of authors for PD-1 and PD-L1 research in the cancer field.

Table 3

The top 10 countries and institutions contributed to publications of PD-1 and PD-L1 research in the cancer field [n (%)].

Rank	Country	N (%)	Institute	N (%)
1	USA	3496 (47.51%)	Univ Texas MD Anderson Canc Ctr (USA)	311 (4.23%)
2	China	1441 (19.58%)	Dana Farber Canc Inst (USA)	280 (3.80%)
3	Japan	832 (11.31%)	Mem Sloan Kettering Canc Ctr (USA)	266 (3.61%)
4	Germany	699 (9.50%)	Harvard Med Sch (USA)	204 (2.77%)
5	France	626 (8.51%)	Johns Hopkins Univ (USA)	193 (2.62%)
6	UK	438 (5.95%)	Brigham & Womens Hosp (USA)	166 (2.26%)
7	Italy	392 (5.33%)	Mayo Clin (USA)	158 (2.15%)
8	Canada	319 (4.33%)	Massachusetts Gen Hosp (USA)	149 (2.02%)
9	Australia	312 (4.24%)	Harvard Univ (USA)	142 (1.93%)
10	South Korea	278 (3.78%)	Univ Penn (USA)	131 (1.78%)

Zhang Y (74, 1.01%), Wolchok JD (66, 0.90%), and Wang Y (63, 0.86%). Among the top 10 co-cited authors, Topalian SL ranked first, with 2919 (0.98%) citations, followed by Robert C (2006 citations, 0.67%), Brahmer JR (1729 citations, 0.58%), Herbst RS (1454 citations,

0.49%), and Hodi FS (1425 citations, 0.48%) while the remaining authors had less than 1400 citations. CiteSpace V was used to create a network of authors and set the threshold to top 50 highly cited articles in a one-year slice [31]. The network map contained 476 nodes and

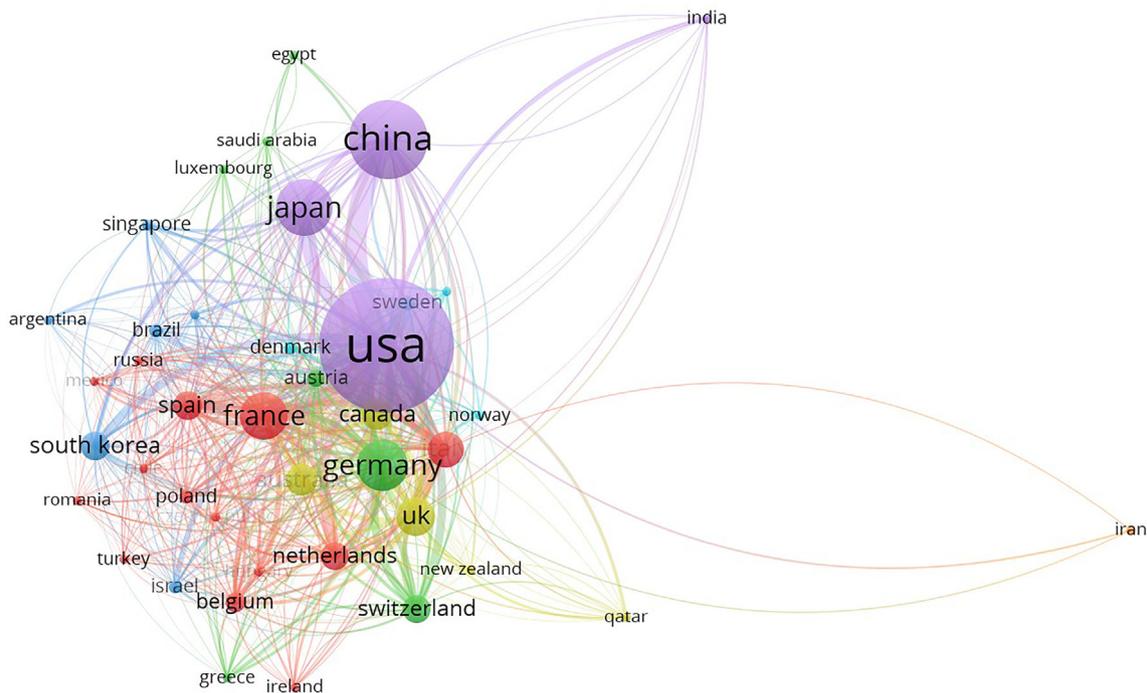


Fig. 4. The network map of countries for PD-1 and PD-L1 research in the cancer field.

1309 links (Fig. 3). Moreover, there were active collaborations among the productive authors.

3.5. Countries and institutions

Publications from Hong Kong, Macau and Taiwan were reclassified to China, and those from England, Scotland, Northern Ireland, and Wales were assigned to the UK. Eighty-eight countries contributed to the publications on PD-1 and PD-L1 research. The top six countries were USA (3496, 47.51%), China (1441, 19.58%), Japan (832, 11.31%), Germany (699, 9.50%), France (626, 8.51%), and UK (438, 5.95%), the other countries published less than 400 articles (Table 3). A network map was created for countries with a frequency greater than 10. As shown in Fig. 4, the map had 41 nodes and 547 links. The 41 countries formed 7 clusters and there were active collaborations between the countries and the clusters.

A total of 6455 institutions contributed to the 7359 papers. The top 10 institutions contributed 2000 (27.18%) articles, and these institutions were all from the USA (Table 3). Among the top 10 institutions, Univ Texas MD Anderson Canc Ctr (311, 4.23%) published the highest number of articles, followed by Dana Farber Canc Inst (280, 3.80%), Mem Sloan Kettering Canc Ctr (266, 3.61%), Harvard Med Sch (204, 2.77%), and Johns Hopkins Univ (193, 2.62%). There were 48 nodes and 753 links in the network map of institutions with a frequency greater than 61 (Fig. 5). The 48 institutions formed 5 clusters, and there were active collaborations among the institutions, especially among the institutions in the same cluster.

3.6. Co-cited references and references with citation bursts

Co-cited references are references that have been co-cited in a set of publications. Table 4 presents the top 10 co-cited references related to PD-1 and PD-L1 research in the field of cancer. The top 10 references were all co-cited more than 740 times. One reference [9] was co-cited more than 1700 times, three references [34–36] were co-cited between 1000 and 1200 times, and six references [14, 37–41] were co-cited between 740 and 1000 times. References with citation bursts are defined as those that are cited frequently over a period of time. In

CiteSpace, the threshold was set to top 50, the minimum duration of the burst was set to five years, from which 80 references with strong citation bursts were detected (Fig. 6). In Fig. 6, the blue line represents the time interval. The time period in which a reference was found to have a burst is displayed by a red line, indicating the first year and the last year of the duration of the burst [33]. References with citation bursts first appeared in 2001, and the strongest burst starting from 2001 is due to a 2000 paper [42]. About 71.25% of the references had citation bursts between 2003 and 2008. The most recent reference [43] with a citation burst appeared in 2013.

3.7. Co-occurrence keywords and cluster analysis

A total of 14,388 keywords were extracted from the 7359 articles. A density map was generated for keywords with the co-occurrence greater than 100 times, which includes 121 keywords in the map (Fig. 7). As shown in Fig. 7 and Table 5, immunotherapy was the most important keyword, with 2035 (2.29%) co-occurrences, followed by cancer (1761, 1.98%), Nivolumab (1468, 1.65%), lung cancer (1438, 1.62%), PD-1 (1358, 1.53%), expression (1340, 1.51%), and PD-L1 (1332, 1.50%). Among the top 20 keywords, some were related to types of cancers such as lung cancer, melanoma, and metastatic melanoma. Others were related to immunotherapies such as Nivolumab, Pembrolizumab, and Ipilimumab. Some were correlated to the mechanism of immunity, such as T-cells and PD-1 blockade.

Clustering analysis was performed for co-occurrence keywords and a network map was created using VOSviewer. Keywords were extracted from titles and abstracts of the 7359 articles. The cumulative frequency of the keywords was calculated and the threshold was set to 40.00% because the keywords with high frequency can accurately reveal the main topic of a field. After calculation, a network map for keywords appearing more than 200 times was generated. There were 68 nodes and 2248 links in the network map, and 68 high-frequency keywords formed 3 clusters (Fig. 8). Cluster 1 included 22 keywords, mainly related to cancer, PD-1, CTLA-4 (Cytotoxic T lymphocyte-associated protein 4), B7-H1 (B7-homolog 1), blockade, t-cells, regulatory t-cells, dendritic cells, and tumor microenvironment. Cluster 2 was the largest cluster which contained 25 keywords, including immunotherapy, lung

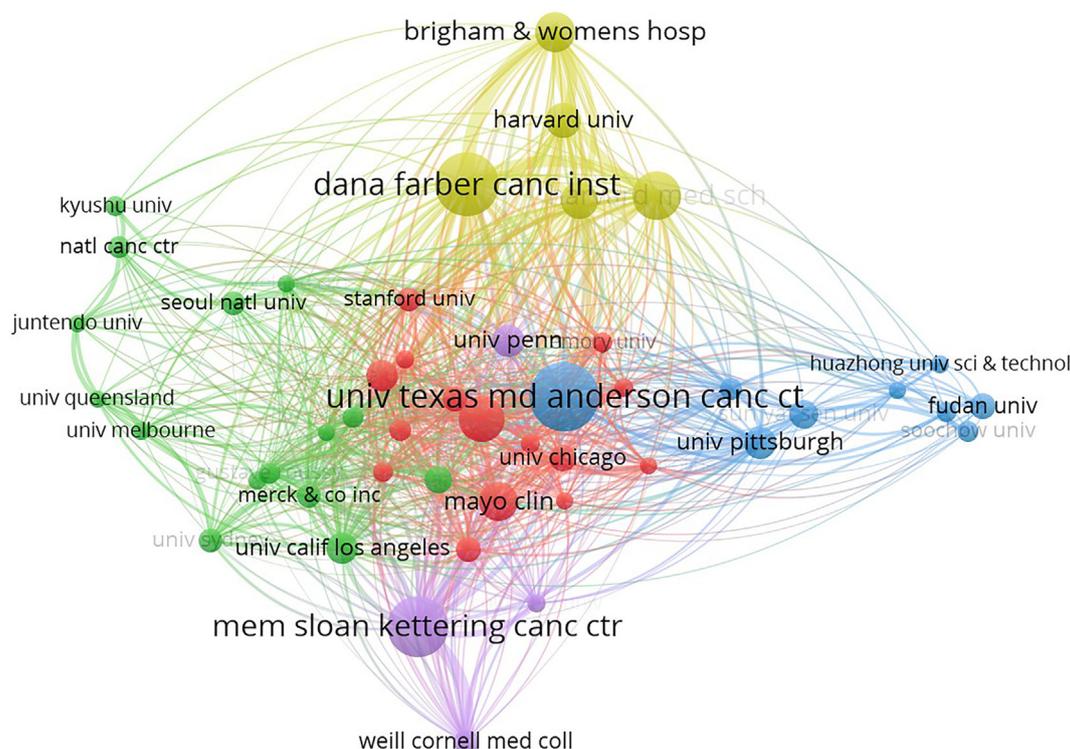


Fig. 5. The network map of institutions for PD-1 and PD-L1 research in the cancer field.

Table 4
Top 10 co-cited references related to PD-1 and PD-L1 research in the cancer field.

Rank	Co-cited reference	Co-citation
1	Topalian SL, 2012, NEW ENGL J MED, V366, P2443. [9]	1764
2	Pardoll DM, 2012, NAT REV CANCER, V12, P252. [34]	1158
3	Brahmer JR, 2012, NEW ENGL J MED, V366, P2455. [35]	1104
4	Hodi FS, 2010, NEW ENGL J MED, V363, P711. [36]	1005
5	Brahmer J, 2015, NEW ENGL J MED, V373, P123. [14]	990
6	Borghaei H, 2015, NEW ENGL J MED, V373, P1627. [37]	986
7	Dong HD, 2002, NAT MED, V8, P793. [38]	857
8	Herbst RS, 2014, NATURE, V515, P563. [39]	809
9	Garon EB, 2015, NEW ENGL J MED, V372, P2018. [40]	758
10	Larkin J, 2015, NEW ENGL J MED, V373, P1270. [41]	747

cancer, nivolumab, melanoma, metastatic melanoma, advanced melanoma, anti-PD-1, checkpoint inhibitors, chemotherapy, and non-small cell lung cancer. Cluster 3 comprised of 21 keywords, mainly related to PD-L1, anti-PD-L1 antibody, immune checkpoint, tumor-infiltrating lymphocytes, breast cancer, colorectal cancer, ovarian cancer, prognosis, and survival.

4. Discussion

In the current study, a comprehensive literature search was conducted in the WoS. A total of 7359 articles which were published in 953 journals in eleven languages were retrieved. The average number of publications per journal was 7.72. In fact, only 17.20% of the journals published more than eight articles. Comparatively, 17.42% of the journals contributed two articles, and 42.29% of journals contributed only one article. This indicates that majority of the journals published a small number of PD-1 and PD-L1 studies. Moreover, no journal was solely focused on publishing PD-1 and PD-L1 research. *Oncoimmunology* was the most productive journal, although it only published 326 articles. Among the top ten journals, six were from the USA, while among the top ten co-cited journals, nine were from the USA, indicating that

American journals not only published a large number of studies but also attracted many co-citations. Only two of the top ten co-cited journals were also among the top ten journals, but seven of the ten co-cited journals had impact factors higher than 10.000, suggesting that the high-impact journals were more frequently co-cited and have a higher influence in this field.

The number of scientific publications reflects the development of a specific area based on bibliometrics [44]. The first PD-1 and PD-L1 research in the cancer field was published in 1991, but before 2003, the number of publications per year was less than 5, which shows that the development of this field was slow during this period. After 2003, the number of publications started increasing, but the annual scholarly output was still less than 100 until 2010. After 2011, the annual scholarly output started growing rapidly, especially after 2014. The number of publications increased from 289 (3.93%) in 2014 to 2705 (36.76%) in 2018. Several important factors contributed to this development in this period. In 2013, *Science Magazine* selected cancer immunotherapy as an annual breakthrough [6]. In 2014, the USA and Japan approved anti-PD-1 antibody (pembrolizumab) for the treatment of advanced metastatic melanoma [45]. In 2016, the FDA approved the anti-PD-L1 antibody (atezolizumab) for the treatment of non-small cell lung cancer and advanced urothelial carcinoma [46,47]. As more PD-1 inhibitors and PD-L1 inhibitors received approval for the treatment of various types of tumors [2], the number of publications continued to grow rapidly.

A total of 40,230 authors contributed to the publication of the 7359 articles, but 69.51% of the authors contributed to the publication of one article. The top ten authors only contributed 8.52% of the papers, and the most productive author published less than 100 articles. This suggests that there were very few productive authors, although many authors were involved. Hodi FS and Wolchok JD were the top ten authors, and they were also among the top ten co-cited authors, indicating that these two authors are key researchers in this field. From the network map of productive authors, it was found that there were active collaborations between the main authors, especially between authors from developed countries.

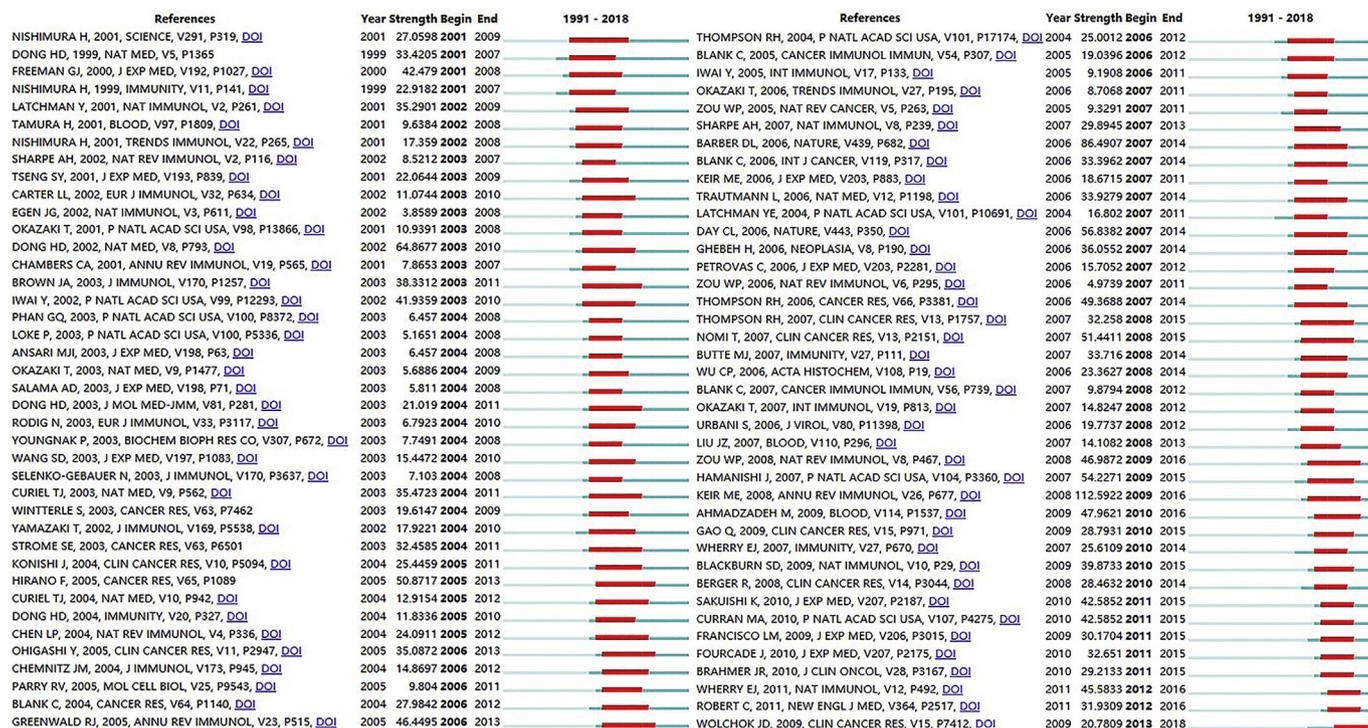


Fig. 6. Top 80 references with strong citation bursts.

Note: The red bars mean some references cited frequently; the green bars were references cited infrequently. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

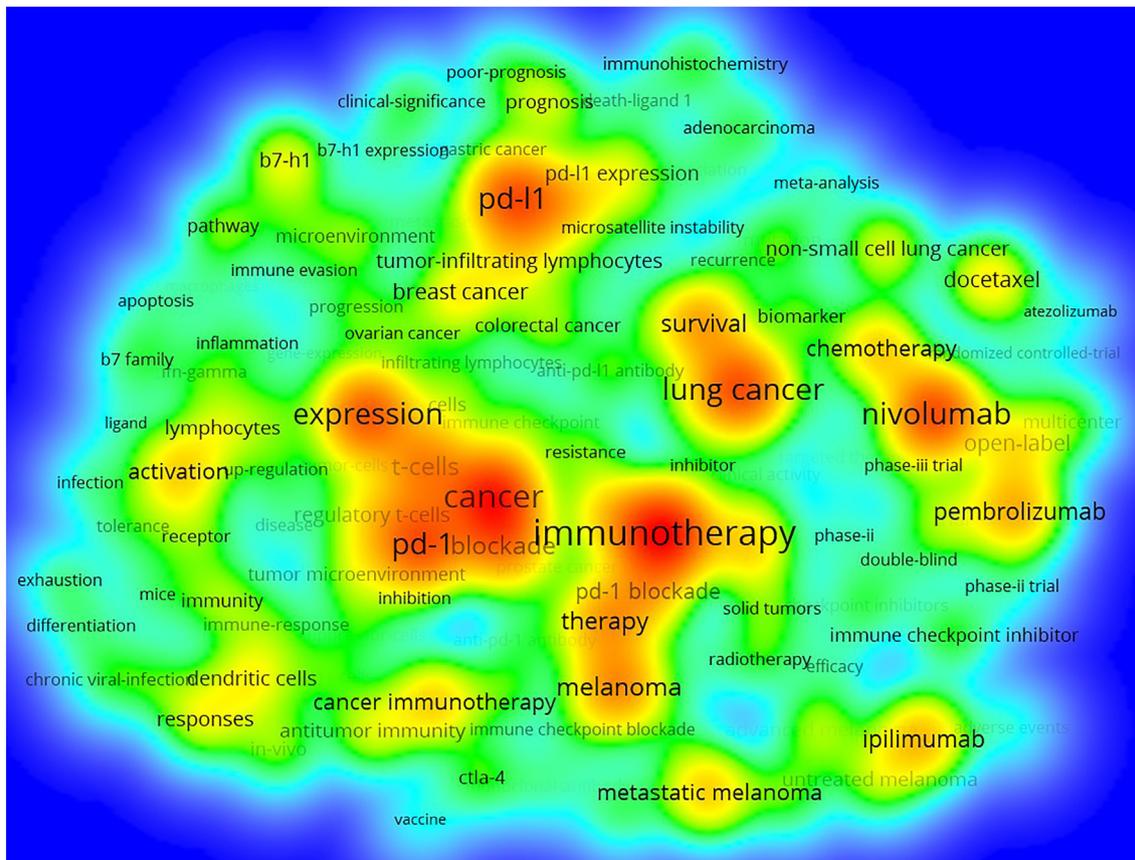


Fig. 7. The density map of keywords for PD-1 and PD-L1 research in the cancer field.

Wolchok et al. in 2009 [43], and the burst is still going on. The authors proposed a new immune-related response standard to assess immunotherapeutic activity in solid tumors [43], which was subsequently used by many scientists as a reference.

14,388 keywords were used in the studies published on PD-1 and PD-L1 research in the field of cancer between 1991 and 2018. However, more than 65.00% of the keywords appeared once, only 6.24% of the keywords had a frequency of greater than ten, revealing that only few keywords are frequently used. In bibliometrics, a network graph of keyword co-occurrences can reflect hot topics [29]. Cluster analysis of co-occurrence keywords showed that there were three clusters in this field. Cluster 1 consisted of 21 keywords, mainly related to the activation and expression of PD-1, CTLA-4, t-cells, regulatory t-cells, and dendritic cells during anti-tumor immunity. PD-1, CTLA-4, t-cells, regulatory t-cells, and dendritic cells play an important role during anti-tumor immunity [51–53]. At present, many scholars are engaged in investigations related to important cells, factors, or checkpoints involved in the process of anti-tumor immunity to promote the development of tumor immunity. Cluster 2 was the largest, consisting of 25 keywords, mainly focused on the use of PD-1 and PD-L1 inhibitors (nivolumab, pembrolizumab) in the immunotherapy of melanoma, non-small cell lung cancer, and lung cancer. Immune checkpoint inhibitors have been widely used in the treatment of various types of tumors and have changed the prospects for advanced cancer treatment [54]. Therefore, the application of PD-1 inhibitors and PD-L1 inhibitors on different tumors has become a hot topic in this field. Cluster 3 includes 21 keywords, mainly related to the survival and prognosis of breast cancer, ovarian cancer, renal cell cancer, and colorectal cancer after treatment with anti-PD-L1 antibody. Although immune checkpoint inhibitors have the potential to treat these conditions, they have been associated with many adverse events, such as diarrhea, colitis, renal injury, hepatitis, and skin toxicity which can be fatal in some cases [54–57]. This had attracted much research attention as scientists endeavor to develop strategies that increase the survival rate of cancer patients after treatment with anti-PD-L1 antibody as well as manage adverse events. From the above analysis, it can be concluded that the trending topics on PD-1 and PD-L1 research in the field of cancer are the efficacy and prognosis of various tumors after treatment with PD-1 inhibitors and PD-L1 inhibitors as well as the activation or expression of important factors during anti-tumor immunity.

4.1. Strengths and limitations

To be the best of our knowledge, this is the first study to perform bibliometric analysis on PD-1 and PD-L1 research in the field of cancer. To comprehensively capture the current status of research on PD-1 and PD-L1, three visualization tools were used to identify the hotspots, cooperation among authors, countries, and institutions in this field. However, this study has some limitations. Firstly, the data was retrieved from WoS only and included research articles. Nevertheless, the amount of data in our analysis is large enough to reflect the current state of PD-1 and PD-L1 research in the field of cancer. Secondly, almost all of the included studies were in English, some related articles in other languages might not have been included [58]. Therefore, it is likely that our results may not be applicable to research published in other languages [59]. Thirdly, since some authors have the same short name, some keywords have different expressions, bias may still exist, although we have standardized them.

5. Conclusions

The number of publications related to PD-1 and PD-L1 research in the field of cancer has been rapidly growing since 2014. *Oncimmunology*, *Oncotarget*, and *Clin Cancer Res* are the top three productive journals. *N Engl J Med*, *J Clin Oncol*, and *Clin Cancer Res* are the top three co-cited journals. Hodi FS and Wolchok JD are among the

top ten authors and the top ten co-cited authors who have the highest influence in this field. Active collaborations were observed among the main authors, especially among authors from developed countries. The USA led in this research field by contributing 47.51% of the total publications. All the top ten institutions were from the USA which have highly promoted the development of PD-1 and PD-L1 research. The productive countries were divided into 7 clusters, the productive institutions were divided into 5 clusters, and there were active collaborations among countries and institutions. The efficacy and prognosis of various tumors after treatment with PD-1 inhibitors and PD-L1 inhibitors as well as the activation or expression of important factors during anti-tumor immunity are the main hot topics.

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Y.G., H.S., and J.T. planned and designed the study. L.G. and J.T. developed the search strategies. Y.G., H.S., W.M., J.C., and Y.C. performed the statistical analysis. L.L., J.W., and J.T. conducted arbitration under disagreement and ensured that there were no errors. Y.G., H.S. and J.T. wrote the first draft. L.G., L.L., and J.T. revised the draft. All authors approved the final version of the manuscript.

Ethics approval and consent to participate

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Consent for publication

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Competing interests

The authors declare that they have no competing interests.

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