The 100 top-cited studies in cancer immunotherapy

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**ABSTRACT**

**Objective:** The objective of the current study was to identify the 100 top-cited studies in cancer immunotherapy.

**Materials and methods:** A retrospective bibliometric analysis was performed in March 2019. Studies were searched on the Web of Science to identify the 100 top-cited studies in cancer immunotherapy. Studies were identified and analysed for authorship, journal, study type, year of publication and institution.

**Results:** The 100 top-cited papers were cited from 591 to 5332 times and were published between 1986 and 2016. They were published in 27 journals, and *New England Journal of Medicine* published most of the studies \((n=14)\), followed by *Nature* \((n=11)\) and *Journal of Clinical Oncology* \((n=10)\). They were published from 10 countries, and the USA published most of the studies \((n=82)\), followed by France \((n=5)\) and Netherlands \((n=3)\). National Cancer Institute in USA was the leading institution and Rosenberg, SA was the most productive author.

**Conclusions:** This study provides insights into development and most important papers in cancer immunotherapy and will provide evidence for future research in cancer immunotherapy.

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**KEYWORDS**
Cancer immunotherapy; bibliometric analysis; citation analysis; top-cited; citation

**Introduction**

Cancer immunotherapy is a therapy used to combat cancer by involving or using the components of the immune system [1]. The current cancer immunotherapy involves three approaches including the blockade of immune checkpoints, adoptive cellular therapy and vaccination [2–5]. In the past 20 years, significant progress has been achieved in cancer immunotherapy. Notably, the Nobel Prize in Physiology or Medicine 2018 awarded the discovery of cancer immunotherapy [6,7]. Up to now, advancements of cancer immunotherapy are mainly reflected by scientific articles, especially by using the bibliometrics analysis [7].

Bibliometrics is an analysis of written publications such as books and articles [8]. It has been used to quantitative research assessment exercise of academic output and provides evidence for funding [9,10]. Citation analysis is the main bibliometrics method [11]. The number of citations is not only the indicator of the impact of an article in the scientific community but also the basis of impact factor [12]. Highly cited papers are considered as the fundamental of research fields [13,14]. Therefore, analysis of highly cited or top cited articles can provide information about scientific progress and research trends in a specific discipline [12].

There have been some studies which were used to assess the top-cited articles in various research fields, such as tuberculosis [15], diabetes [16], surgery [17], anaesthesiology [18], rehabilitation [19], vaccine [20], etc. However, no such study for cancer immunotherapy has been published. Therefore, we performed the current bibliometric analysis to assess the 100 top-cited articles for cancer immunotherapy.

**Materials and methods**

This was a retrospective bibliometric analysis which did not involve human subjects [12], thus it was not needed to be approved by the institutional review board.

**Search strategy**

We performed a search of studies in cancer immunotherapy in Web of Science Core Collection on 10 March 2019. The searched terms included cancer and immunotherapy. All papers since 1945 in the database were searched. The searched results were sorted by citations and articles which had more citations ranked higher [13].

**Article selection**

Two authors independently screened the abstracts and full-texts to identify the 100 top-cited articles about cancer immunotherapy.
immunotherapy. Disagreements were resolved by discussion. Only articles that focused on the subject of cancer immunotherapy were included. A cancer immunotherapy article was defined as any study that focused on any immunotherapy for any cancer. Articles about studies conducted using other therapy for cancer but mentioned immunotherapy was excluded. In addition, studies that analysed the immune factors which have potential effect for cancer were also excluded.

**Data extraction**

After all 100 top-cited articles were selected, data were extracted by two authors [13]. The following data were extracted [13], including title, citation number, publication year, number of authors, name of first author and corresponding author, source journal, impact factor of the journal, article types.

**Data analysis**

Data analyses were performed to determine study type, country, year of publication, journal title, authorship, institution, as previously described [13]. All of the data were presented by using only descriptive statistics, and no statistical significance tests were performed [12].

**Results**

The 100 top-cited articles are listed in Table 1. The 100 top-cited articles were identified on the basis of their citations, and the number of citations ranged from 591 to 5332 with a total number of citations equal to 103,763 and a median number of citations equal to 812.5.

These papers were published in 27 journals (Table 2). The highest number was from the *New England Journal of Medicine* (n = 14), followed by *Nature* (n = 11) and *Journal of Clinical Oncology* (n = 10). Other journals like *Science Translational Medicine*, *Nature Reviews Cancer*, *Journal of Experimental Medicine*, *Nature Medicine* and *Nature Reviews Immunology* had at least five but less than 10 articles. The other 19 journals had less than five articles. The impact factors of all the journals ranged from 4.225 to 79.26.

All articles were published during a span of 31 years from 1986 to 2016 (Table 3). The maximum number of articles were published in 2011 and 2012 (n = 9), and for a five-year period, the maximum contribution was made by 2011–2015 (n = 32).

Of all the 100 articles, 72 articles were original articles, 28 were reviews (Table 4). Among the 72 original articles, there were 43 basic researches, 28 trials and one case report. The average citations of trials were much higher those of the basic researches.

A total of 10 countries contributed to the top 100 cited articles (Table 5). The USA contributed most of the articles with 83 papers, France contributed five papers, while Argentina, China, Australia, Belgium, England, Germany, Japan and Netherlands each contributed less than five studies.

Among the 100 articles, 17 institutions contributed more than one article (Table 6). The 17 institutions were from four countries, including USA (n = 14), France (n = 1), Netherlands (n = 1) and Belgium (n = 1). The top four contributors were National Cancer Institute in USA (n = 21), Johns Hopkins University in USA (n = 6), Baylor Institution Immunology Research in USA (n = 4) and French National Institute of Health and Medical Research in France (n = 4).

There were 11 authors contributed more than one article as first author, and 12 authors contributed more than one article as the corresponding author (Table 7). Rosenberg, SA contributed the highest number of papers as both corresponding author (n = 13) and first author (n = 8).

**Discussion**

Given the high burden of cancer, there has been great productivity of cancer research. In the past two decades, cancer immunotherapy is the most promising research field for the treatment of cancer. Although there have been several citation analyses concerning various cancers [117–119], yet there has been no such study for cancer immunotherapy to describe the research trends. Given cancer immunotherapy awarded by Nobel Prize last year, thus, we performed the current study.

The top 100 most-cited articles were published in 33 different journals between 1986 and 2016. *New England Journal of Medicine* was the most frequent journal in our list, with 14 articles, followed by *Nature* and *Journal of Clinical Oncology*. Other top journals include *Science Translational Medicine*, *Nature Reviews Cancer*, *Journal of Experimental Medicine*, *Nature Medicine* and *Nature Reviews Immunology*.

Our study encompasses a wide variety of authors, institutions and countries. The USA had a powerful influence, 83% of articles were originated from the institution in that country, whereas the other several countries contributed the remaining papers. When we examined the publications by individual authors, we found Rosenberg SA contributed most of the top-cited papers as first author and corresponding author. It is very surprising that both the two Nobel prize winners James P. Allison and Tasuku Honjo were not listed in top-cited papers as contact author and first author. In the 100 top-cited papers, there were only four papers co-authored by Allison [41,46,89,99], while there was no paper co-authored by Tasuku Honjo. It was possible that their papers might have not so many citations. However, their papers would be cited more time in the next few years, because everyone knows them now and would like to cite their studies.

Like many previous bibliometric analyses, our study also has some limitations [120]. First, citation analysis was based on the Web of Science, citation numbers might be misleading [11,120], owing to self-citations, sub-publications and time of publications, we may have missed some important papers which have been indexed by other databases, such as Scopus and Google [19]. Second, as for the authorship, we only included the first author and corresponding author. It is possible that several authors will have co-authored papers.
### Table 1. The 100 top-cited studies in cancer immunotherapy.

| Title                                                                 | Journal                           | Article type | Total citation | Publication year | Page number | PMID       |
|----------------------------------------------------------------------|-----------------------------------|--------------|----------------|------------------|-------------|------------|
| Safety, activity, and immune correlates of anti-PD-1 antibody in cancer [4] | New England Journal of Medicine   | Trial        | 5332           | 2012             | 12          | 22658127  |
| The blockade of immune checkpoints in cancer immunotherapy [21]       | Nature Reviews Cancer             | Review       | 3887           | 2012             | 13          | 22437870  |
| Safety and activity of anti-PD-L1 antibody in patients with advanced cancer [3] | New England Journal of Medicine   | Trial        | 3440           | 2012             | 11          | 22658128  |
| Ipilimumab immunotherapy for castration-resistant prostate cancer [22] | New England Journal of Medicine   | Trial        | 2759           | 2010             | 12          | 20818862  |
| Vaccination of melanoma patients with peptide or tumor lysate-pulsed dendritic cells [23] | Nature Medicine                   | Basic research | 2349 | 1998 | 5 | 9500607 |
| Tumor-associated B7-H1 promotes T-cell apoptosis: a potential mechanism of immune evasion [24] | Nature Medicine                   | Basic research | 2290 | 1998 | 7 | 12091876 |
| Cancer immunotherapy: moving beyond current vaccines [25]             | Nature Medicine                   | Review       | 1912           | 2004             | 7           | 15340416  |
| Cancer regression and autoimmunity in patients after clonal repopulation with antitumor lymphocytes [26] | Science                           | Basic research | 1868 | 2002 | 6 | 12242449 |
| Safety and tumor responses with lambrolizumab (anti-PD-1) in melanoma [27] | New England Journal of Medicine   | Trial        | 1855           | 2013             | 11          | 23724846  |
| Chimeric antigen receptor-modified T cells in chronic lymphoid leukemia [28] | New England Journal of Medicine   | Trial        | 1631           | 2011             | 9           | 21830940  |
| Cancer regression in patients after transfer of genetically engineered lymphocytes [29] | Science                           | Basic research | 1530 | 2006 | 4 | 16946036 |
| Immunologic and therapeutic evaluation of a synthetic peptide vaccine for the treatment of patients with metastatic melanoma [30] | Nature Medicine                   | Basic research | 1476 | 1998 | 7 | 9500606 |
| Genetic basis for clinical response to CTLA-4 blockade in melanoma [31] | New England Journal of Medicine   | Trial        | 1460           | 2014             | 11          | 25409260  |
| Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial [32] | Lancet                           | Trial        | 1445           | 2016             | 11          | 26712084  |
| A new approach to the adoptive immunotherapy of cancer with tumor-infiltrating lymphocytes [33] | Science                           | Basic research | 1412 | 1986 | 4 | 3489291 |
| Phase I study of single-agent anti-programmed death-1 (MDX-1106) in refractory solid tumors: safety, clinical activity, pharmacodynamics, and immunologic correlates [34] | Journal of Clinical Oncology      | Trial        | 1390           | 2010             | 9           | 20516446  |
| Cancer immunotherapy comes of age [35]                                | Nature                            | Review       | 1303           | 2011             | 10          | 22193102  |
| Constant-infusion recombinant interleukin-2 in adoptive immunotherapy of advanced cancer [36] | New England Journal of Medicine   | Trial        | 1292           | 1987             | 8           | 3493433  |
| Immunosuppressive networks in the tumour environment and their therapeutic relevance [37] | Nature Reviews Cancer             | Review       | 1268           | 2005             | 12          | 15776005  |
| Production of vascular endothelial growth factor by human tumors inhibits the functional maturation of dendritic cells [38] | Nature Medicine                   | Basic research | 1187 | 1996 | 8 | 8837607 |
| Intraepithelial CD8(+) tumor-infiltrating lymphocytes and a high CD8(+) regulatory T cell ratio are associated with favorable prognosis in ovarian cancer [39] | Proceedings of the National Academy of Sciences of the United States of America | Basic research | 1182 | 2005 | 6 | 16344461 |
| Effector memory T cells, early metastasis, and survival in colorectal cancer [40] | New England Journal of Medicine   | Basic research | 1125 | 2005 | 13 | 16371631 |
| The future of immune checkpoint therapy [41]                          | Science                           | Review       | 1093           | 2015             | 6           | 25838373  |
| Neoantigens in cancer immunotherapy [42]                              | Science                           | Review       | 1092           | 2015             | 6           | 25838375  |
| MPDL3280A (anti-PD-L1) treatment leads to clinical activity in metastatic bladder cancer [43] | Nature                            | Basic research | 1082 | 2014 | 12 | 25428503 |
| Adoptive cell transfer therapy following non-myeloablative but lymphodepleting chemotherapy for the treatment of patients with refractory metastatic melanoma [44] | Journal of Clinical Oncology      | Trial        | 1065           | 2005             | 12          | 15800326  |
| Survival, durable tumor remission, and long-term safety in patients with advanced melanoma receiving nivolumab [45] | Journal of Clinical Oncology      | Trial        | 1056           | 2014             | 12          | 24590637  |
| Cancer regression and autoimmunity induced by cytotoxic T lymphocyte-associated antigen 4 blockade in patients with metastatic melanoma [46] | Proceedings of the National Academy of Sciences of the United States of America | Basic research | 1049 | 2003 | 6 | 12826605 |
| Tumor-antigens recognized by t-lymphocytes [47]                       | Annual Review of Immunology       | Review       | 1030           | 1994             | 29          | 8011285  |

(continued)
| Title                                                                 | Journal                                      | Article type  | Total citation | Publication year | Page number | PMID          |
|----------------------------------------------------------------------|----------------------------------------------|---------------|----------------|------------------|-------------|---------------|
| Induction of tumor immunity by removing CD25(+)CD4(+) T cells: a common basis between tumor immunity and autoimmunity [48] | *Journal of Immunology*                      | Basic research | 1022           | 1999             | 8           | 10553041      |
| Prevalence of regulatory T cells is increased in peripheral blood and tumor microenvironment of patients with pancreas or breast adenocarcinoma [49] | *Journal of Immunology*                      | Basic research | 1006           | 2002             | 6           | 12193750      |
| Oncology meets immunology: the cancer-immunity cycle [50]           | *Immunity*                                   | Review        | 995            | 2013             | 10          | 23890059      |
| Nephrectomy followed by interferon alfa-2b compared with interferon alfa-2b alone for metastatic renal-cell cancer [51] | *New England Journal of Medicine*            | Trial         | 995            | 2001             | 5           | 11759643      |
| Progress in human tumour immunology and immunotherapy [52]         | *Nature*                                     | Review        | 994            | 2001             | 5           | 11357146      |
| Bone-marrow-derived dendritic cells pulsed with synthetic tumor peptides elicit protective and therapeutic antitumor immunity [53] | *Nature Medicine*                            | Basic research | 985            | 1995             | 6           | 7489412       |
| Myeloid-derived suppressor cells: linking inflammation and cancer [54] | *Journal of Immunology*                      | Review        | 982            | 2009             | 8           | 19342621      |
| Crosstalk between cancer and immune cells: role of STAT3 in the tumour microenvironment [55] | *Nature Reviews Immunology*                  | Review        | 975            | 2007             | 11          | 17186030      |
| T cells with chimeric antigen receptors have potent antitumor effects and can establish memory in patients with advanced leukemia [56] | *Science Translational Medicine*             | Basic research | 972            | 2011             | 11          | 21832238      |
| Vaccination with Mage-3A1 peptide-pulsed mature, monocyte-derived dendritic cells expands specific cytotoxic T cells and induces regression of some metastases in advanced stage IV melanoma [57] | *Journal of Experimental Medicine*           | Basic research | 965            | 1999             | 10          | 10587357      |
| Immunosuppressive strategies that are mediated by tumor cells [58]  | *Annual Review of Immunology*                | Review        | 954            | 2007             | 30          | 17134371      |
| Case report of a serious adverse event following the administration of T cells transduced with a chimeric antigen receptor recognizing ERBB2 [59] | *Molecular Therapy*                          | Case report   | 907            | 2010             | 9           | 20179677      |
| Durable complete responses in heavily pretreated patients with metastatic melanoma using T-cell transfer immunotherapy [60] | *Clinical Cancer Research*                   | Trial         | 898            | 2011             | 8           | 21498393      |
| Treatment of 283 consecutive patients with metastatic melanoma or renal-cell cancer using high-dose bolus interleukin-2 [61] | *JAMA-Journal of the American Medical Association* | Trial         | 877            | 1994             | 7           | 8120958       |
| Adoptive cell transfer: a clinical path to effective cancer immunotherapy [62] | *Nature Reviews Cancer*                      | Review        | 862            | 2008             | 10          | 18354418      |
| Cancer immunotherapy via dendritic cells [1] Tumor-associated macrophages: from mechanisms to therapy [63] | *Nature Reviews Cancer*                      | Review        | 860            | 2012             | 13          | 22437871      |
| *Dendritic cells as therapeutic vaccines against cancer [64]         | *Nature Reviews Immunology*                  | Review        | 840            | 2005             | 11          | 15803149      |
| Characterization of circulating T cells specific for tumor-associated antigens in melanoma patients [65] | *Nature Medicine*                            | Basic research | 831            | 1999             | 9           | 10371507      |
| Natural innate and adaptive immunity to cancer [66]                 | *Annual Review of Immunology*                | Review        | 829            | 2011             | 37          | 21219185      |
| Results of treatment of 255 patients with metastatic renal-cell carcinoma who received high-dose recombinant interleukin-2 therapy [67] | *Journal of Clinical Oncology*               | Trial         | 814            | 1995             | 9           | 7884429       |
| Radical nephrectomy plus interferon-alfa-based immunotherapy compared with interferon alfa alone in metastatic renal-cell carcinoma: a randomised trial [68] | *Lancet*                                     | Trial         | 811            | 2001             | 5           | 11583750      |
| Adoptive immunotherapy for cancer: harnessing the T cell response [69] | *Nature Reviews Immunology*                  | Review        | 794            | 2012             | 13          | 22437939      |
| Identification of a human-melanoma antigen recognized by tumor-infiltrating lymphocytes associated with in-vivo tumor rejection [70] | *Proceedings of the National Academy of Sciences of the United States of America* | Basic research | 785            | 1994             | 5           | 8022805       |
| Tumor regression in patients with metastatic synovial cell sarcoma and melanoma using genetically engineered lymphocytes reactive with NY-ESO-1 [71] | *Journal of Clinical Oncology*               | Trial         | 773            | 2011             | 8           | 21282551      |
| Title                                                                 | Journal                                      | Article type | Total citation | Publication year | Page number | PMID          |
|----------------------------------------------------------------------|----------------------------------------------|--------------|----------------|------------------|-------------|---------------|
| Treatment of established renal-cancer by tumor-cells engineered to secrete interleukin-4 [72] | Science                                      | Basic research | 767            | 1991             | 4           | 1948050      |
| Regression of metastatic renal-cell carcinoma after nonmyeloablative allogeneic peripheral-blood stem-cell transplantation [73] | New England Journal of Medicine              | Trial        | 753            | 2000             | 9           | 10984562     |
| Immunological aspects of cancer chemotherapy [74]                     | Nature Reviews Immunology                    | Review       | 751            | 2008             | 15          | 18097448     |
| Therapy of murine tumors with tumor peptide-pulsed dendritic cells: dependence on T cells, B7 costimulation, and T helper cell 1-associated cytokines [75] | Journal of Experimental Medicine             | Basic research | 750            | 1996             | 11          | 8551248      |
| Differential regulation of folate receptor isoforms in normal and malignant-tissues in-vivo and in established cell-lines – physiological and clinical implications [76] | Cancer                                       | Basic research | 738            | 1994             | 12          | 7513252      |
| Gene therapy with human and mouse T-cell receptors mediates cancer regression and targets normal tissues expressing cognate antigen [77] | Blood                                        | Basic research | 727            | 2009             | 12          | 19451549     |
| Cetuximab-induced anaphylaxis and IgE specific for galactose-alpha-1,3-galactose [78] | New England Journal of Medicine              | Basic research | 720            | 2008             | 9           | 18337601     |
| Placebo-controlled phase III trial of immunologic therapy with sipuleucel-T (APC8015) in patients with metastatic, asymptomatic hormone refractory prostate cancer [79] | Journal of Clinical Oncology                 | Trial        | 720            | 2006             | 6           | 16809734     |
| CD40 agonists alter tumor stroma and show efficacy against pancreatic carcinoma in mice and humans [80] | Science                                      | Basic research | 714            | 2011             | 5           | 21436454     |
| Identification of the immunodominant peptides of the MART-1 human-melanoma antigen recognized by the majority of HLA-A2-restricted tumor-infiltrating lymphocytes [81] | Journal of Experimental Medicine             | Basic research | 713            | 1994             | 6           | 7516411      |
| B-cell depletion and remissions of malignancy along with cytokine-associated toxicity in a clinical trial of anti-CD19 chimeric-antigen-receptor-transduced T cells [82] | Blood                                        | Trial        | 711            | 2012             | 12          | 22160384     |
| Recombinant human interleukin-2, recombinant human interferon alfa-2a, or both in metastatic renal-cell carcinoma [83] | New England Journal of Medicine              | Trial        | 708            | 1998             | 7           | 9562581      |
| Cytokines in cancer pathogenesis and cancer therapy [84]              | Nature Reviews Cancer                        | Review       | 696            | 2004             | 12          | 14708024     |
| Maintenance bacillus Calmette-Guerin immunotherapy for recurrent Ta, T1 and carcinoma in situ transitional cell carcinoma of the bladder: a randomized Southwest Oncology Group study [85] | Journal of Urology                           | Trial        | 695            | 2000             | 6           | 10737480     |
| Metronomic cyclophosphamide regimen selectively depletes CD4(+) CD25(+) regulatory T cells and restores T and NK effector functions in end stage cancer patients [86] | Cancer Immunology                            | Immunotherapy | 688            | 2007             | 8           | 16960692     |
| Human gene MAGE-3 codes for an antigen recognized on a melanoma by autologous cytolytic T-lymphocytes [87] | Journal of Experimental Medicine             | Basic research | 681            | 1994             | 10          | 8113684      |
| Blockade of B7-H1 improves myeloid dendritic cell-mediated antitumor immunity [88] | Nature Medicine                              | Basic research | 680            | 2003             | 6           | 12704383     |
| Checkpoint blockade cancer immunotherapy targets tumour-specific mutant antigens [89] | Nature                                       | Basic research | 671            | 2014             | 18          | 25428507     |
| Mechanisms and functional significance of tumour-induced dendritic-cell defects [90] | Nature Reviews Immunology                    | Review       | 662            | 2004             | 12          | 15573129     |
| Combining immunotherapy and targeted therapies in cancer treatment [91] | Nature Reviews Cancer                        | Review       | 660            | 2012             | 15          | 22437869     |
| Activity and safety of nivolumab, an anti-PD-1 immune checkpoint inhibitor, for patients with advanced, refractory squamous non-small-cell lung cancer (CheckMate 063): a phase 2, single-arm trial [2] | Lancet Oncology                              | Trial        | 660            | 2015             | 9           | 25704439     |
| Loss of tumor suppressor PTEN function increases B7-H1 expression and immunoresistance in glioma [92] | Nature Medicine                              | Basic research | 658            | 2007             | 5           | 17159987     |
| Title                                                                 | Journal                          | Article type | Total citation | Publication year | Page number | PMID      |
|----------------------------------------------------------------------|----------------------------------|--------------|----------------|------------------|-------------|-----------|
| Immune and clinical responses in patients with metastatic melanoma to CD34(+) progenitor-derived dendritic cell vaccine [93] | Cancer Research                  | Basic research | 646            | 2001             | 8           | 11522640  |
| Management of immune-related adverse events and kinetics of response with ipilimumab [94] | Journal of Clinical Oncology     | Review       | 642            | 2012             | 7           | 22614989  |
| Virus-specific T cells engineered to coexpress tumor-specific receptors: persistence and antitumor activity in individuals with neuroblastoma [95] | Nature Medicine                  | Basic research | 640            | 2008             | 7           | 18978797  |
| Immune surveillance of tumors [96]                                    | Journal of Clinical Investigation | Review       | 639            | 2007             | 10          | 17476343  |
| Treatment of patients with metastatic melanoma with autologous tumor-infiltrating lymphocytes and interleukin-2 [97] | Journal of the National Cancer Institute | Trial       | 635            | 1994             | 8           | 8028037   |
| Radiation and dual checkpoint blockade activate non-redundant immune mechanisms in cancer [98] | Nature                           | Basic research | 633            | 2015             | 18          | 25754329  |
| Biologic activity of cytotoxic T lymphocyte-associated antigen 4 antibody blockade in previously vaccinated metastatic melanoma and ovarian carcinoma patients [99] | Proceedings of the National Academy of Sciences of the United States of America | Basic research | 633            | 2003             | 6           | 12682289  |
| Genomic correlates of response to CTLA-4 blockade in metastatic melanoma [100] | Science                          | Basic research | 629            | 2015             | 5           | 26359337  |
| Indoleamine 2,3-dioxygenase and tumor-induced tolerance [101]         | Journal of Clinical Investigation | Review       | 626            | 2007             | 8           | 17476344  |
| Ipilimumab monotherapy in patients with pretreated advanced melanoma: a randomised, double-blind, multicentre, phase 2, dose-ranging study [102] | Lancet Oncology                  | Trial        | 623            | 2010             | 10          | 20004617  |
| Radiation modulates the peptide repertoire, enhances MHC class I expression, and induces successful antitumor immunotherapy [103] | Journal of Experimental Medicine | Basic research | 622            | 2006             | 13          | 16636135  |
| Inducible apoptosis as a safety switch for adoptive cell therapy [104] | New England Journal of Medicine  | Trial        | 615            | 2011             | 11          | 22047558  |
| Safety and persistence of adoptively transferred autologous CD19-targeted T cells in patients with relapsed or chemotherapy refractory B-cell leukemias [105] | Blood                            | Basic research | 614            | 2011             | 12          | 21849486  |
| Overall survival analysis of a phase ii randomized controlled trial of a poxviral-based PSA-targeted immunotherapy in metastatic castration-resistant prostate cancer [106] | Journal of Clinical Oncology      | Trial        | 611            | 2010             | 7           | 20100959  |
| Mutations associated with acquired resistance to PD-1 blockade in melanoma [107] | New England Journal of Medicine  | Basic research | 608            | 2016             | 11          | 27433843  |
| Tumor regression and autoimmunity after reversal of a functionally tolerant state of self-reactive CD8+ T cells [108] | Journal of Experimental Medicine | Basic research | 607            | 2003             | 12          | 12925674  |
| Talmigene laherparepvec improves durable response rate in patients with advanced melanoma [109] | Journal of Clinical Oncology      | Trial        | 606            | 2015             | 13          | 26014293  |
| CD4(+)CD25(+) regulatory T cells suppress tumor immunity but are sensitive to cyclophosphamide which allows immunotherapy of established tumors to be curative [110] | European Journal of Immunology    | Basic research | 605            | 2004             | 9           | 14768038  |
| Monoclonal antibodies: versatile platforms for cancer immunotherapy [111] | Nature Reviews Immunology         | Review       | 602            | 2010             | 11          | 20414205  |
| Monoclonal antibodies against the 4-1BB T-cell activation molecule eradicate established tumors [112] | Nature Medicine                  | Basic research | 601            | 1997             | 4           | 9176498   |
| Targeting the PD-1/B7-H1(PD-L1) pathway to activate anti-tumor immunity [113] | Current Opinion in Immunology    | Review       | 595            | 2012             | 6           | 22236695  |
| Intratumoral balance of regulatory and cytotoxic T cells is associated with prognosis of hepatocellular carcinoma after resection [114] | Journal of Clinical Oncology      | Basic research | 592            | 2007             | 8           | 17577038  |
| Adoptive immunotherapy for cancer: building on success [115]          | Nature Reviews Immunology         | Review       | 592            | 2006             | 11          | 16622476  |
| Up-regulation of PD-L1, IDO, and T-regS in the melanoma tumor microenvironment is driven by CD8(+) T cells [116] | Science                          | Basic research | 591            | 2013             | 10          | 23986400  |
### Table 2. Journals of the 100 top-cited studies published.

| Journal | Total citation | Number of study | Average citation | Impact factor (2017) |
|---------|----------------|-----------------|------------------|---------------------|
| New England Journal of Medicine | 23,293 | 14 | 1664 | 79.26 |
| Nature | 4683 | 11 | 426 | 32.621 |
| Journal of Clinical Oncology | 8269 | 10 | 827 | 26.36 |
| Science Translational Medicine | 1563 | 8 | 195 | 41.058 |
| Nature Reviews Cancer | 8233 | 7 | 1176 | 41.982 |
| Journal of Experimental Medicine | 4338 | 6 | 723 | 10.790 |
| Nature Medicine | 13,609 | 6 | 2268 | 42.784 |
| Nature Reviews Immunology | 5216 | 5 | 1043 | 41.577 |
| Proceedings of the National Academy of Sciences of the United States of America | 3649 | 4 | 912 | 9.504 |
| Annual Review of Immunology | 2813 | 3 | 938 | 22.714 |
| Blood | 2052 | 3 | 684 | 15.132 |
| Journal of Immunology | 3010 | 3 | 1003 | 4.539 |
| Immunity | 1842 | 2 | 921 | 19.734 |
| Journal of Clinical Investigation | 1265 | 2 | 633 | 13.251 |
| Lancet Oncology | 1283 | 2 | 642 | 53.254 |
| Lancet | 2256 | 2 | 1128 | 36.421 |
| Science | 9105 | 2 | 4553 | 16.710 |
| Cancer Immunology Immunotherapy | 688 | 1 | 688 | 9.130 |
| Cancer Research | 646 | 1 | 646 | 6.537 |
| Cancer | 738 | 1 | 738 | 4.225 |
| Clinical Cancer Research | 898 | 1 | 898 | 10.199 |
| Current Opinion in Immunology | 595 | 1 | 595 | 7.932 |
| European Journal of Immunology | 605 | 1 | 605 | 4.248 |
| JAMA-Journal of the American Medical Association | 877 | 1 | 877 | 47.661 |
| Journal of the National Cancer Institute | 635 | 1 | 635 | 11.238 |
| Journal of Urology | 695 | 1 | 695 | 5.381 |
| Molecular Therapy | 907 | 1 | 907 | 7.008 |

### Table 3. Published years of the 100 top-cited studies.

| Year | Number of study | Total citation | Average citation |
|------|-----------------|----------------|------------------|
| 1986 | 1 | 1412 | 1412 |
| 1987 | 1 | 1292 | 1292 |
| 1991 | 1 | 767 | 767 |
| 1994 | 7 | 3441 | 492 |
| 1995 | 2 | 1799 | 900 |
| 1996 | 2 | 1937 | 969 |
| 1997 | 1 | 5459 | 5459 |
| 1998 | 3 | 1448 | 483 |
| 1999 | 3 | 3446 | 1149 |
| 2000 | 2 | 601 | 301 |
| 2001 | 4 | 3875 | 969 |
| 2002 | 3 | 5164 | 1721 |
| 2003 | 4 | 5480 | 1370 |
| 2004 | 4 | 3464 | 866 |
| 2005 | 5 | 1709 | 342 |
| 2006 | 4 | 5132 | 1283 |
| 2007 | 7 | 5116 | 731 |
| 2008 | 4 | 2973 | 743 |
| 2009 | 2 | 4533 | 2267 |
| 2010 | 6 | 8349 | 1392 |
| 2011 | 9 | 4713 | 524 |
| 2012 | 9 | 2053 | 228 |
| 2013 | 3 | 2969 | 990 |
| 2014 | 5 | 6892 | 1378 |
| 2015 | 6 | 16,921 | 2820 |
| 2016 | 2 | 2818 | 1409 |

### Table 4. Study types of the 100 top-cited studies.

| Study type | Number of study | Total citation | Average citation |
|------------|-----------------|----------------|------------------|
| Original article | 72 | 75,781 | 1053 |
| Basic research | 43 | 39,644 | 922 |
| Trial | 28 | 35,230 | 1258 |
| Case report | 1 | 907 | 907 |
| Review | 28 | 27,982 | 999 |

### Table 5. Countries of the 100 top-cited studies.

| Country | Number of studies | Total citation | Average citation |
|---------|------------------|----------------|------------------|
| Argentina | 1 | 954 | 954 |
| Australia | 1 | 639 | 639 |
| Belgium | 2 | 1711 | 856 |
| China | 1 | 592 | 592 |
| England | 1 | 1082 | 1082 |
| France | 5 | 3877 | 775 |
| Germany | 2 | 3314 | 1657 |
| Japan | 1 | 1022 | 1022 |
| Netherlands | 3 | 2525 | 842 |
| USA | 83 | 88,047 | 1061 |

### Table 6. Institutions published at least two 100-top cited studies.

| Institution | Country | Number of study |
|-------------|---------|-----------------|
| National Cancer Institute | USA | 21 |
| Johns Hopkins University | USA | 6 |
| French National Institute of Health and Medical Research | France | 4 |
| Baylor Institution Immunology Research | USA | 4 |
| University of Pennsylvania | USA | 4 |
| Dana-Farber Cancer Institute | USA | 3 |
| Memorial Sloan Kettering Cancer Center | USA | 3 |
| University of California, San Francisco | USA | 3 |
| Washington University | USA | 3 |
| Ludwig Institute for Cancer Research | Belgium | 2 |
| Netherlands Cancer Institution | Netherlands | 2 |
| Southwest Oncology Group | USA | 2 |
| Tulane University | USA | 2 |
| University of California, Los Angeles | USA | 2 |
| University of Pittsburgh | USA | 2 |
| University of South Florida | USA | 2 |
| University of Texas | USA | 2 |
and therefore be underrepresented in the current study [11]. Third, searching based on title and contents means a small number of manuscripts which involving cancer immunotherapy might not have been identified [12].

In conclusion, our study provides a comprehensive list of the true landmark publication in cancer immunotherapy and recognize contributions made by essential authors, institutions, published scientific journals, research types. Given the high burden of cancer, cancer immunotherapy remains an important research area. Increased research productivity is clearly indicated on numerous fronts of cancer immunotherapy.

Disclosure statement

No potential conflict of interest was reported by the authors.

Ethics committee approval

This is a bibliometric analysis, so ethics approval is not applicable.

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