Peer Review File

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Reviewer A

A Bibliometric Analysis of Wnt Signaling pathway: From the Top-100 Cited Articles to Emerging Trends

First of all, I would like to thank the opportunity to review this manuscript. This study was a bibliometric analysis of the top 100 most-cited papers and all papers published within the last decade about Wnt signaling pathway. After reviewing the manuscript, some concerns were raised and they are listed below along with other comments:
Reply: We are very grateful for your comments regarding our manuscript. We have studied comments carefully and have made corrections which we hope meet with approval.

Comment 1: Minor comments
Some typos and errors were found in the text. Please carefully review the entire manuscript to correct them.
Reply1: With the help of language checker "Grammarly" and a native English speaker, we reviewed the entire manuscript and carefully corrected previous typos and errors as advised.
Changes in the text: see the Language Editing part in editorial comments.

Comment 2: Abstract
The background does not clearly state the aim of the study.
It is important to inform the date of the search since citation count are modified daily.
In results, it would be interesting to present some data about main countries, institutions and authors.
Reply2: We have added a statement of our research objective in the background, the search date in the methods, and presented data about main countries and authorships in the results as advised. Considering the conciseness of the abstract, data about main institutions were not listed here. (see line 25, 28, 33)
Changes in the text: "By analyzing these studies' characteristics and qualities, we aim to reveal the current research focus and emerging trends in Wnt signaling."
"… to identify articles on May 23rd, 2020"
"These articles were published mainly from 2000 to 2009 (62%). Citations per article ranged from 599 to 3780 with a median number of 880 times. Most studies (66%)

came from the United States. Nusse Roel and Clevers Hans (15 and 13 papers) have contributed significantly to the field. The most highlighted study themes were cancer (15%), embryo development (14%), and cytoplasm signal transduction (11%)."

Comment 3: Introduction
I think authors could go deeper explaining more about citations. What does this mean? What is the importance of citation count? How bibliometric can be used to evaluate a topic?
Reply3: We added explanations on the importance of citation count and the evaluation usage of bibliometric methods in the introduction. (see line 69)
Changes in the text: "During the analyzing process, basic characteristics of identified manuscripts were first extracted. Then the quality and distribution of manuscripts were evaluated using statistical methods and analyzing tools. Citation analysis was one of its key methodologies. Citation number received by manuscripts is viewed as a marker for its importance and is reflected in the impact factor of journals. Generally, high-cited articles provided the basis for their field, and growing citation counts often mean emerging focuses."

Comment 4: Materials and Methods/Results
It is not clear the database choice: WoS "All Databases" includes: WoS-CC, KCI, Russian and SciELO Citation Index. Did authors use WoS "All Databases" in the search? Or they searched individually in each database?
Reply4: We used WoS and selected WOS CC, BIOSIS Citation Index, KCI-Korean Journal Database, MEDLINE, Russian Science Citation Index, and SciELO Citation Index in the database options of WOS. We have modified the statements to clear our database choice. (see line 89)
Changes in the text: "Articles were identified by searching in the ISI Web of Science database (Thomson Reuters, New York, the United States). We selected WOS Core Collection, BIOSIS Citation Index, KCI-Korean Journal Database, MEDLINE, Russian Science Citation Index, and SciELO Citation Index in WOS to retrieve all articles related to Wnt."

Comment 5: In addition, MEDLINE does not furnish citation count. I think that this database was used only to retrieve all papers in the last decade, but it is confusing. I suggest authors to individualize which databases were searched to retrieve the top 100 most-cited papers and which databases were searched to retrieve all papers in the last decade. If they mixed all databases in a unique result, it is quite confusing. Why authors decided to follow this approach?
Reply5: MEDLINE was also included in WOS. We search manuscripts in MEDLINE

via WOS. In this way, WOS furnished us with their citation count data. In fact, we searched the same Database portfolio with the same search terms to retrieve the top 100 most-cited papers and all papers in the last decade. We believed this strategy maintained our research's consistency, so that our prediction of the emerging trends is accurate. We have emphasized this point in the text as advised. (see line 109)
Changes in the text: "Meanwhile, we analyzed all articles within the last ten years in the Wnt field. For research's consistency and an accurate prediction of emerging trends, we used the same Database portfolio and search terms as above. By limiting the publication date to the last decade (2011 to 2020), we retrieved 41337 articles."

Comment 6: Also, as many databases were searched, why not to search in Scopus?
Reply6: We have three main reasons for searching in WOS.
(1) Compared with Web of Science, Scopus retrieved more citations from non-English-language sources and review, and fewer citations from articles, editorials, and letters [Kulkarni AV, Aziz B, Shams I, et al. Comparisons of citations in Web of Science, Scopus, and Google Scholar for articles published in general medical journals. Jama 2009;302:1092-6.].
Our analysis focused on English-language manuscripts, so WOS was enough and suitable.
(2) WOS covers the oldest publications, because its indexed and archived records go back to 1900. Scopus includes articles published from 1966, but information regarding citation analysis is available only for articles published after 1996 [Falagas ME, Pitsouni EI, Malietzis GA, et al. Comparison of PubMed, Scopus, Web of Science, and Google Scholar: strengths and weaknesses. Faseb j 2008;22:338-42.].
Since study on Wnt started in 1982, we used WOS to avoid missing key manuscripts.
(3) The internal search tool of WOS allowed us to acquire data, including self-citation and citations in last five years, more conveniently.
We have added discussion on this in the limitation as advised. (see line 380)
Changes in the text: "3) our analysis focused on English-language manuscripts, data from non-English-language sources was omitted."

Comment 7: In which paper authors based on to include just the 275 top cited papers?
Reply7: During our first round of exclusion based on rank of citations, N Tang and JQ Xu have reviewed the title and abstract of identified articles. After the 275 top-cited articles were retrieved, we estimated that there had been enough top 100 articles that meet the inclusion criteria. To reduce the number of articles necessitating subsequent screening, we conduct the subsequent analysis on the 275 articles. We have revised our statement as advised. (see line 95)

Changes in the text: “After reviewing the title and abstract, the 275 top-cited articles cited were included to reduce the number of articles necessitating subsequent screening…”

Comment 8: Who guarantee that all of these papers were focused on Wnt signaling? In my opinion, authors should read and analyze all papers until reach the top100 most-cited papers that clearly focused on Wnt signaling.
Reply8: We estimated that there had been enough top 100 articles that meet the inclusion criteria among 275 articles screened in the 1st round. Then in the 2nd round, two independent investigators, N Tang and JQ Xu, which major in the field, carefully read and analyzed the content of the 275 included articles at the same time. 131/275 articles were qualified to meet the criteria. Finally, in the 3rd round, 100/131 were included through re-ranking. We have revised our statement as advised. (see line 98)
Changes in the text: “Two independent investigators read and analyzed the whole content of the 275 included articles at the same time to enhance the screening sensitivity.”

Comment 9: Eligibility criteria is not clear. Authors reported that they included papers which considered Wnt as the research core. So, if this type of paper was included, how authors could exclude paper which content was not related to Wnt or which Wnt was not the central focus of the topic?
Reply9: We carefully checked the title and content of each article. For example, an article (from 275 articles screened in the 1st round) could be searched through our search terms [Schwitalla S, Fingerle AA, Cammareri P, et al. Intestinal Tumorigenesis Initiated by Dedifferentiation and Acquisition of Stem-Cell-like Properties. Cell 2013;152:25-38.
]. Times cited on May 23rd, 2020: 543
However, it only mentions Wnt as downstream signaling of NF-kappa B in the article; elevated NF-kappa B signaling enhanced Wnt activation. The actual research object is NF-kappa B's function in tumor-initiating cells. The article meets our eligibility criteria 2)Wnt which is not the central focus of the topic.
Other examples include:

1. Bailey P, Chang DK, Nones K, et al. Genomic analyses identify molecular subtypes of pancreatic cancer. Nature 2016;531:47-+. Times cited: 869
2. Wood AR, Esko T, Yang J, et al. Defining the role of common variation in the genomic and biological architecture of adult human height. Nature Genetics 2014;46:1173-86. Times cited: 823
3. Aragona M, Panciera T, Manfrin A, et al. A Mechanical Checkpoint Controls Multicellular Growth through YAP/TAZ Regulation by Actin-Processing Factors.

Cell 2013;154:1047-59. Time cited: 628

Comment 10: For n>50, Kolmogorov-Smirnov test is better recommended than Shapiro-Wilk test.
Reply10: We utilized the Kolmogorov-Smirnov test in IBM SPSS Statistics 22.0 to re-test the distribution of individual variables for normality. The result of our analysis was not altered. We have revised our statement in the statistical analysis part as advised. (see line 130)
Changes in the text: "The Kolmogorov-Smirnov test was used to test the distribution of individual variables for normality."

Comment 11: How country and institution were determined? Based on the affiliation of the corresponding author? This needs to be clear stated.
Reply11: We determined country and institution based on the affiliation of the corresponding author. When there are multiple affiliations of corresponding author, the institution of first author was utilized. We have emphasized this point in the text as advised. (see line 119)
Changes in the text: "The geographic origin, research institution and department were determined based on the affiliation of the corresponding author. When there are multiple affiliations of corresponding author, the institution of first author was utilized."

Comment 12: How themes were determined?
Reply12: After carefully reviewing the top-100 articles, our group gained a more comprehensive understanding of the field. We first listed some common topics, including cancer, embryo development, cytoplasm signal transduction, stem cells, osteogenesis, and noncanonical pathways. Then we read and analyzed articles one by one to determine its theme. During this process, a number of themes were added. Besides, some articles include more than two topics. For example, the themes of "Wnt proteins are lipid-modified and can act as stem cell growth factors" were "protein purification and stem cells"
We have added our strategy of theme determination in the text as advised. (see line 122)
Changes in the text: "We carefully reviewed all articles and used two or three words to summarize and categorize each article's themes adequately."

Discussion
This section is adequate.

Reviewer B

The authors of the manuscript entitled “A Bibliometric Analysis of Wnt Signaling pathway: From the Top-100 Cited Articles to Emerging Trends” (ID: ATM-21-174), performed a study with a bibliometric approach in order to concur on the top 100 cited articles in the last decade regarding the Wnt signaling pathway. The article presents a topic of interest, in light of the exceptional contributing role of the Wnt signaling pathway towards a wide range of scientific fields, along with the existence of a great number of published articles failing to evaluate the quality of the evidence provided by them.

The manuscript appears to be well-structured and both abstract and introduction section are well-written and comprehensive, with the latter to include adequate references to support the respective evidence. Methodology and statistical analysis appear valid. Results are clearly presented and outlined in both text, Tables, and Figures. Discussion is inclusive, and reader-friendly, as well as clearly stating the limitations of this study.

Reply: We are very grateful for your comments regarding our manuscript. We have studied comments carefully and have made corrections which we hope meet with approval.

Comment 13: Minor comments are with respect to further highlighting the novelty of the study in the “introduction” section

Reply13: We have carefully modified our “introduction” section to further highlighting the novelty of the study as advised. (see line 70, 79)

Changes in the text: “Then the quality and distribution of manuscripts were evaluated using statistical methods and analyzing tools. Citation analysis was one of its key methodologies. Citation number received by manuscripts is viewed as a marker for its importance and is reflected in the impact factor of journals. Generally, high-cited articles provided the basis for their field, and growing citation counts often mean emerging focuses(18,19).”

“However, few bibliometric studies analyzed both the top-cited and most recent studies. And a comprehensive analysis of the overall Wnt field remains to be completed.”

Comment 14:, along with increasing the quality of Figure 2, as it probably incommodes the readership. Finally, in Figure 4, the authors should correct the “Fig.7” of the sentence “The size…terms” by converting it to “Fig 4. (A)” or perhaps “(A)”.

Reply14: We have increased the quality of Figure 1-3 as advised (Adobe Illustrator

options: resolution high 300ppi, optimization of words). We have corrected the "Fig.7" of the sentence "The size…terms" by converting it to "Fig 4. (A)" as advised and recheck the correctness of all diagram annotation. **(see Figure 1-4)**