

Peer Review File

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Reviewer A

Major Comments:

Comment 1: The title of the article suggests outcomes are based on tissues but the vast majority of investigations appear to be in-vitro in nature and little on periodontal and peri-implant tissues per-say. Trends described are more in the area of research in periodontics and dental implantology, not tissues. For example, many studies references are in-vitro studies on cells. Comment is warranted.

Reply 1: We gratefully thanks for the precious time the reviewer spent making this constructive comment, which we think is very important to this article. This article did analyze the past and present research of miRNA in periodontology and implant dentistry, and this was our original goal. After discussion, we think that the misuse of tissues may be due to different understandings of tissues in different cultural contexts (my native language and English). From the title, we have revised all the relevant expressions in the article to make them more consistent with the purport of the article. In addition, we also construct a new search query containing words such as implant dentistry to check if there are any omissions in the first search. Under the same time range and retrieval conditions, there are only three different articles between two search results (we think this is mainly due to the use of wildcards in the first search). After further reading the title and abstract, we excluded these three articles according to the original exclusion criteria, because their research has nothing to do with microRNA. Therefore, we are confident that this revision of the expression will not have any impact on the original results and conclusions.

Changes in the text: We have modified our text (see Page1, line 1, 22; Page 3, line 41; Page 6, line 107; Page 12, line 221; Page 15, line 302; Page 20, line 410; Page 22, line 449; Page 23, line 472, 479; Page 36, line 689).

Comment 2: Similarly, there is lack of focus on type of study, such as in-vitro (cells, 3D cultures, etc.) and in-vivo research (animal, human). How many of these studies are derived from clinical data (biopsies, GCF, saliva, etc.) or from animal studies. What about studies related to differences in miRNA before and after an intervention such as periodontal or peri-implantitis therapy? What are the trends and hot spots in these areas? This will be clearly different from in-vitro studies which appears to be the main focus of the manuscript. Lack of this information limits what can be concluded from this manuscript and may bias results/conclusions.

Reply 2: We gratefully appreciate for your valuable comment. Like other bibliometric analysis, one of the limitations of this article is that there is less attention to the specific content of the research than the traditional literature review. The traditional literature review puts more emphasis on content and pays more attention to the content and shortcomings of the existing research. Bibliometrics analysis is a systematic analysis of all (from hundreds to tens of thousands) papers in a field using statistics methods. Its purpose is to reveal the current research hotspots and future development trends, as well as landmark papers to help researchers who have just entered this field to grasp the overall trend in this field. However, different types of research have different focuses, and ignoring these differences may lead to misjudgment of research hotspots and trends. It is necessary to point out this question and remind interested researchers. We are very grateful to your comments, which provides new ideas for our future research work.

Changes in the text: We have added a limitation at Page 23, line 467.

Comment 3: What are the trends/hotspots in bioinformatics and data analysis? This is a critical important when large data sets are to be analyzed. What are the limitations?

Reply 3: We totally understand the reviewer's concern. Identifying what trends/hotspots are is critical to bioinformatics and data analysis.

Bioinformatics combines biology, computer science, information engineering, mathematics and statistics to analyze and interpret the biological data. Literature analysis, a type of bioinformatics analysis, aims to use computational and statistical linguistics to mine this growing text database.

Bibliometrics analysis is similar to literature analysis, and their research objects are literatures. The difference is that literature analysis pays more attention to biomedical text mining, such as abbreviation recognition, named entity recognition and so on. Bibliometrics, or Scientometrics, is often used in the field of library science and information science. Most of the research contents are literature records, such as the publication year, keywords, authors, number of citations, references and so on.

The author believes that in bibliometric analysis, topics with a large number of studies can be called hotspots, especially the collection of studies that are frequently cited together. Different periods can have different research hotspots. Only the recent research hotspots can be called research trends.

This paper mainly determines the research hotspots and trends through citation analysis and topic analysis. As in the discussion (see Page 22, line 460), time lag is one of the most important limitations. The recently published literature often lacks sufficient citations, so it is difficult to form an ideal co-citation network. We have read the literature of the last three years one by one to eliminate this error as much as possible.

Comment 4: How does research focus of investigators, particularly those with more

publications in the field, impact the results and conclusions of this article? Do they skew the data and suggested trends/hotspots as a result of their strong interests in a specific area? Are they actual hotspots in the field or more like specific research interests? A discussion is warranted.

Reply 4: We gratefully appreciate for your valuable advice. As mentioned in reply3, CiteSpace mainly uses co-citation analysis to determine research hotspots/trends. Its specific principle is: If two papers are both cited by many other papers, they have a stronger relationship. The more papers they are cited by, the stronger their relationship is. Each cluster represents an interrelated literature network, and cluster's labels indicating the research hotspot/trend is composed of representative keywords in the citing literature. This analysis method can avoid the influence of productive authors on the data and results to a certain extent. However, the author's motivation for citing other people's literature may not always be academic-related, which may bias the results of the analysis. For example, some scholars have observed that scientists tend to cite research from friends more frequently. And those publications that have already received a high reputation tend to get more trust, thus being cited in future research.

Changes in the text: We have added a discussion at Page 21, line 425.

Comment 5: Similarly, is the lack of direct cooperation between institutions/countries perhaps simply due to differences in research interests? The authors should speculate as to why differences occur.

Reply 5: Thank you for your precious comment and advice. To be more clearly and in accordance with the reviewer concerns, we have added speculation about the reasons for the lack of direct cooperation between productive research groups and differences in research interests.

Changes in the text: We added our speculations at Page 13, line 250 and Page14, line 280.

Minor Comments:

Comment 1: Numerous syntax errors are noted. The manuscript would benefit by a secondary review to eliminate these errors.

Reply 1: Thank you for your careful review. We are very sorry for the mistakes in this manuscript and inconvenience they caused in your reading. The manuscript has been thoroughly revised and rewritten by two English language editors from AME Editing Service, so we hope it can meet the journal's standard.

Changes in the text: Details of the changes can be found in markup of Jones and J. Chapnick in track changes manuscript.

Comment 2: Please check sentence on p5, line 13 for accuracy. I believe the authors

meant to say periodontitis have a higher incidence of peri-implantitis.

Reply 2: Thank you so much for your careful check. This is a clerical error. We are sorry that we did not examine the manuscript carefully enough.

Changes in the text: We have modified our text (see Page5, line 77).

Reviewer B

Minor Comments:

Comment 1: The reviewer recommends the authors to summaries better in their conclusions what are their recommendations on how to advance the research in the field.

Reply 1: We gratefully appreciate for your valuable comment. To be more clearly and in accordance with this study's aim, we have added a more detailed interpretation regarding conclusions.

Changes in the text: We have added our text as advised (see Page 24, line 489).

Comment 2: Also, please revise the acknowledgement section to be written more professionally.

Reply 2: Thank you for your careful review. We are very sorry for this expression and inconvenience they caused in your reading. The manuscript has been thoroughly revised and rewritten by professional English editors.

Changes in the text: We have modified our text at Page 25, line 495.