

Peer Review File

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Reviewer A:

Overall

The analysis is based on all publications present in the Web of Science database and containing the words “mTOR (or mammalian target of rapamycin)” and “kidney”. The output is very diversified, including all sort of bibliometric information: institutions, authors, years and keywords. The review is mostly intended for researchers that approach the topic for the first time and want to get a glimpse of the major institutions/authors that have worked in the field in the past or at present, the Countries that are mainly involved, and milestone publications in the field. The analysis also provides connections of these items in time and space, exploiting the citations. These connections are intended as a tool to interpret where a discovery comes from and how it has expanded and influenced other discoveries. The analysis is interesting and useful, but only partially fulfill its aims. Recommendations for improving the manuscript are listed below.

[Reply: We would like to thank the reviewer who has provided constructive feedback and suggestions that have greatly improved our manuscript. We have added reviewer's suggestions in this revised manuscript. Each of the comments have been addressed in a point-to-point as follows.](#)

Comment #1: In the first paragraph, the authors give basic numbers, such as tot. number of publications that match the criteria (“mTOR” AND “kidney”), year of the first publication, number of publications per year, citations, etc.

[Reply #1: Thank you for your comments.](#)

Comment #2: These data would be much more informative if inserted in a bigger frame and compared with other areas of research. For example: “Only after 2005 did the articles on mTOR reach at least a double-digit number annually”. Is this a delay

compared to other areas of research? I'd like to have some comparisons to guide my judgement. Considering that the manuscript needs to be restricted to a specific topic, I suggest that the authors provide the same information given in the paragraph "annual publications and trend", but concerning the literature that contains "mTOR" only and "kidney" only.

Reply #2: We appreciate your constructive comment. We inserted these data in a bigger frame and compared with the literature that contains "mTOR" only and "kidney" only. In the past 20 years, the proportion of mTOR pathway in the overall research of kidney showed an upward trend. The comparative analysis of "mTOR (or mammalian target of rapamycin)" and "kidney", "mTOR" only and "kidney" only has been painted and added in the revised manuscript (Figure 2A).

Changes in the text: We have modified our text as advise (see Page 6, line 16-17 and Figure 2A).

Comment #3: Table 1 and 2 ranks institutions and journals with the highest number of articles. I'd like to see the same table, but with a ranking based on number of citations, which better represent the impact of research.

Reply #3: Thank you for your constructive comment. As you said, number of citations can better represent the impact of research.

Changes in the text: Table 1 and 2 ranks institutions and journals with the highest number of citations (see Table1 and Table 2).

Comment #4: The analysis of keywords (Figure 4) is probably the more interesting. Authors use it to picture the main fields of research in the area and their evolution over time (Figure 4E and F).

Reply #4: Thanks for your comments. Figure 4 has been separated into Figure 4 and 5.

Changes in the text: Figure 4E and 4F were changed to pictures 5A and 5B respectively.

Comment #5: But I would be curious to see other interesting developments that are not addressed. For example, among the hotspots in figure 4C and D there are multiple

names of drugs (rapamycin, sirolimus, everolimus, cyclosporine). I think that a detailed analysis of the drugs that come up from the analysis would be of interest, in particular bursts of citations mentioning a specific drug over the years and associations with specific pathologies. Some analyses can be done for signaling pathways. These analyses can really point out trends in research/therapy and specific areas that are worth studying, but are not covered yet.

Reply #5: Thank you for your suggestions. As shown in Figure 5A, B, we show research focuses about mTOR signaling pathway in kidney disease. Future research hotspots will embody in diabetic nephropathy, kidney transplantation, autosomal dominant polycystic kidney disease, tuberous sclerosis complex, renal cell carcinoma and autophagy. And according to your suggestions, we analyze drugs and associations with specific diseases and add corresponding discussion in the revised manuscript (Figure 4C, D).

Changes in the text: The corresponding discussion has been added in the revised manuscript (see Page 13, line 4-10).

Comment #6: Figures are generally small and hard to read. I understand that they need to report a lot of information in a very small size, but at least the font size in figure 4B should be increased. Figure 4H is potentially very interesting, but I could not read it. It would be better presented as a bigger figure on its own.

Reply #5: We appreciate your constructive comments and have modified the quality of figures.

Changes in the text: We have modified our figures as advised (see Figure 2, Figure 3, Figure 4 and Figure 5).

Comment #7: Figure 2C is described as: “According to the heat map made by VOSviewer revealed that the USA Germany and China had the most intense publication density” in the results section. Please, correct the sentence, “revealed that” should be removed. The hotspot representing Italy seems equally strong and I see no reasons for

not mentioning this Country.

Reply #7: We are really sorry for the error and have corrected it in the revised manuscript.

Changes in the text: We have added the related discussion in the revised manuscript (see Page 7, line 5-6).

Comment #8: In the abstract: Research hot spots include “diabetic nephropathy” “kidney transplantation” “autosomal dominant polycystic kidney disease” “tuberous sclerosis complex” “renal cell carcinoma” and “autophagy”. Seven key clusters are detected including kidney transplantation”. Clusters of what? And what is the difference with the research hot spots mentioned before? Please clarify also in the corresponding section of methods and results.

Reply #8: Thank you for these suggestive comments. Based on CiteSpace, the co-citation network was segmented into fourteen subsets from the titles of the cited articles and the largest seven clusters include “kidney transplantation” “autosomal dominant polycystic kidney disease” “renal transplantation” “renal cell carcinoma” “hamartin” “autophagy” and “tuberous sclerosis complex”. But research hot spots are excavated from term timeline and keywords timeline. And the timeline view shows the occurrence, popularity, and decline of research subjects. Meanwhile, clusters reflected the temporal characteristics of the research areas in timeline view. In the section of “Results”, we have clarified in the corresponding section (see Page 9, line 19-20 and Page 10, line 1-6).

Comment #9: Methods/ Data source and search strategy: “TXT format which allowed for the analyzation of bibliometric tools”: analysis.

Reply #9: Thank you for this comment. The bibliometric tools of CiteSpace and VOSviewer can only analyze data of TXT format.

Reviewer B:

Comment #1: It would be interesting if the manuscript were part of a more extensive

investigation, including at least comparative analysis, critical conclusions, or something similar.

Reply #1: Thanks for your suggestion. We have added more detailed investigation about mTOR signaling pathway in kidney disease in the revised manuscript according to your valuable suggestions.

Changes in the text: We have modified our text as advise (see Page 6, line 16-17 and Figure 2A).

Comment #2: Why did the authors choose the mTOR signaling pathway? It is not clear.

Reply #2: Thank you for the constructive comment. Since the discovery of rapamycin's primary target molecular mode of action and the functional biology effect, mTOR has been recognized to permeate many areas of medicine and increasing evidence indicates that mTOR pathway plays a significant role in transplantation, homeostasis, metabolism, and regeneration in the kidney (13-16). We compared with the literature that contains "mTOR" only and "kidney" only. In the past 20 years, the proportion of mTOR pathway in the overall research of kidney showed an upward trend. For new researchers to this area, bibliometric analysis can be helpful to follow the current study focuses and overall trends and reveal landmark literatures in the field.

13. Fantus D, Rogers NM, Grahammer F, et al. Roles of mTOR complexes in the kidney: implications for renal disease and transplantation. *Nat Rev Nephrol* 2016;12:587-609.

14. Shiels PG, McGuinness D, Eriksson M, et al. The role of epigenetics in renal ageing. *Nat Rev Nephrol* 2017;13:471-82.

15. Orhon I, Dupont N, Zaidan M, et al. Primary-cilium-dependent autophagy controls epithelial cell volume in response to fluid flow. *Nat Cell Biol* 2016;18:657-67.

16. Grahammer F, Nesterov V, Ahmed A, et al. mTORC2 critically regulates renal potassium handling. *J Clin Invest* 2016;126:1773-82.