Reviewer 3 Comments

Review on the manuscript "Nanoparticle-Mediated Modulation of Tumor-Associated Macrophages: A Frontier in Cancer Therapy" by Xuejia Kang et al.

According with the literature data, in cancer therapy, targeting tumor-associated macrophages has shown promise. In addition, the control over the tumor-associated macrophages with the help of nanoparticles led to improved therapeutic effect. This review is focused on the tumor-associated macrophages capability to influence the tumor microenvironment and on the effect of the nanoparticles over the tumor-associated macrophages; even do the title underlines the "nanoparticle-mediated modulation" of tumor-associated macrophages. Maybe the authors should reconsider the title or the review's objectives. The review is interesting, but I have some questions that I think the authors should consider:

RESPONSE: Thank you for the encouraging and positive comments. Based on your suggestion, we have changed the title of the manuscript. The revised title: Tumor-Associated Macrophage Targeting of Nanomedicines in Cancer Therapy.

The abstract should underline the main finding of this review.

RESPONSE: Thank you for this suggestion. We revised the abstract by adding the main findings of the review in the revised manuscript.

What protocol was used when were selected the studies included in this review?

RESPONSE: We searched the keyword including "Tumor-associated macrophage, Suppressive immune environment, Tumor proliferation and metastasis, Nanomedicine, Targeted delivery systems." in google scholar, web of science, PubMed, and extracted the key points and presented this review. This information has been included in the revised manuscript.

Please present the databases or other resources used to identify the studies. Were used some criteria or limitations in this process? How were these studies selected?

RESPONSE: This review was compiled from the published articles through November 2023 from various databases such as PubMed, Google Scholar, Web of Science. We searched the keywords including "Tumor-associated macrophage, Suppressive immune environment, Tumor proliferation and metastasis, Nanomedicine, Targeted delivery systems." and manually extracted the key points and presented this review. This information has been included in the revised manuscript.

Did the authors consult the PRISMA guidelines?

RESPONSE: PRISMA is mostly used with clinical research, while it can be applied to systematic reviews in other fields as well. We used the guiding principles of PRISMA in our review.

The introduction is to short, has nearly a page. All the sections until section 6 should be reorganized as subsections of the introduction.

RESPONSE: Thank you for this valuable comment. We have expanded the introduction. Authors appreciate this suggestion; the review becomes more logical and readable.

Please use the same abbreviation in the manuscript, for example M2 TAMs, m2 TAMs or M2TAMs.

RESPONSE: Thank you, we regret the inconsistency in the presentation. we have changed throughout the entire manuscript.

Some of the figures are practically illegible, please carefully verify them.

RESPONSE: Thank you for pointing out this. Yes, we have corrected the figure4 and figure 6 and will make sure all the figures will be of highest quality in the final publication.

What are the limitations of the review?

RESPONSE: Because the macrophage is a double-edge sword, thus, an accurate balance of M1 and M2 is important. The excessive M1 is beneficial for anti-cancer, however, it will also cause a bad influence including the cytokine release syndrome that is commonly adverse impact of immunotherapy. Considering the topic and the contents, we have not included the part: controversial roles of M1 and relative strategies ,but we mentioned in the part 7, suggesting the importance of monitoring the cytokine storm. All this information has been provided in the revised manuscript.