



**Baishideng  
Publishing  
Group**

7901 Stoneridge Drive, Suite 501,  
Pleasanton, CA 94588, USA  
**Telephone:** +1-925-223-8242  
**Fax:** +1-925-223-8243  
**E-mail:** bpgoffice@wjgnet.com  
**https://**www.wjgnet.com

## PEER-REVIEW REPORT

**Reviewer's code:** 00504187

### COMMENTS TO AUTHORS

This manuscript is a huge and very detailed up-to-dated description of the present role of macrophages in gastrointestinal disorders. The article is so long and possibly exhaustive that for those not deeply involved in this field it might be difficult at the end to have a relatively clear understanding of the most critical functions of these cells. From the conclusion, we know that they are indispensable to suppress inflammation and play an essential role in maintaining homeostasis. Moreover their role in IBD and gastrointestinal tumor may be relevant but needs to be clarified. This I think is the message. As said above, the paper would be more acceptable if more concise and if , from the huge amount of data reported, it could be extrapolated or selected and emphasized the most critical ones. English language could also be improved. Nevertheless the paper is certainly a complete review of a relatively unfamiliar issue for gastroenterologists and is worth of publication, with some revisions concerning mainly a more succinct and better summarizing construction. Looking at some details:

- Introduction is too long. The last paragraph (from the word "In general") could be avoided

**Response:** According to your kind suggestion, we have already truncated the introduction. Please check the last paragraph of the introduction (line 11-14, page 5). Thanks.

- At the first page of Introduction, line 13 from below, the word "insignificant" should probably be "significant"

**Response:** Thank you for your great suggestion. According to our manuscript (line 2 from below, page 22), the macrophages do play an important role in such complex condition. We think that you may be confused by the detailed description of the extremely intricate situation. But what we want to emphasize is that even in such a complex condition, where so many immune cells do their jobs, the macrophages still have significant function of immunoregulation. Thanks.

- The reference 139, which is cited twice in the text, (Mantovani A, Allavena P. The interaction of anticancer therapies with tumor-associated macrophages. The Journal of experimental medicine 2015; 212(4): 435-445) should be cited correctly with the surnames of the authors (Mantovani and Allavena) and not with their names (Alberto and Paola)

**Response:** Thank you for your kind suggestion. We have already modified the reference. Please check them (line 5, page 20 and line 7, page 21). Thanks.



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**https://**[www.wjgnet.com](http://www.wjgnet.com)

• In the Conclusions, the statement: “However, they do not show weak microbicidal activities” is not clear to me. Does it mean that they show a strong microbicidal activity? In such case, the second form may be preferable. Even the word “microbicidal” is not correct.

**Response:** Thank you for your great suggestion. We substituted the original word “microbicidal” to “bactericidal” and also changed the sentence into “they show a strong bactericidal activities”. Please check line 2 from below, page 22. Thanks.

**Reviewer’s code:** 00058401

#### **COMMENTS TO AUTHORS**

Congratulations for the quality of yours manuscript.

No response. Thanks.

**Reviewer’s code:** 00503442

#### **COMMENTS TO AUTHORS**

I read with great interest the Review Article entitled “Functional macrophages and gastrointestinal disorders” by Yue-Hong Liu et al. The manuscript is interesting. Although the Authors stated that their manuscript is aimed to discuss the potential role of macrophages in IBD and neoplastic disease, this second section is poorly represented. One alternative is that the Authors focus their manuscript on IBD rather than IBD and cancer.

**Response:** Thank you for your great suggestion. We consider that although the second section is relatively poor-represented compared with the first part, cancer have close relationship with immune cells, including the macrophages. Moreover, we hope that this part can inspire the further and incisive researches about treatment of neoplastic disease. Therefore, we hope that whether there is any possibility to keep it. Thanks.