

Dear Editor:

We are pleased to resubmit for publication the revised version of “*Role of tumor associated macrophages in regulating pancreatic cancer progression*” (ESPS Manuscript #21752). We appreciated the constructive criticisms of the reviewers. We have addressed each of their concerns as outlined below. We have also highlighted any changes made in the revised manuscript. Please also note revised title of the manuscript.

Reviewer #1:

The abstract describes very little about the content of the review, apart from a general statement in the last sentence. I believe that the readers need to be given more content being covered.

The abstract have been revised to give readers a better understanding of the content being covered in the manuscript.

I have concerns that the references are not an update of the field with only a couple of references for 2014. Indeed there have been many papers published in 2015 and not one of these has been mentioned. This is an opportunity to provide the latest views in this Journal.

We have included citations of recently published papers that contribute to our topic (page 7, page 9, page 10, page 12, page 13, page 14). However, much of the data that contributes to our understanding of the topic has been published prior to 2015.

I was a little disappointed that the role of tolerogenic and immunogenic DCs was not well covered but just toughed on. Is there any avenue for this. In autoimmune inflammatory diseases such as rheumatoid arthritis there is an interest to inject tolerogenic DCs in patients. Is there any view to injecting immunogenic DCs in cancer?

We find this topic very interesting and, indeed, our laboratory is interested in the topic of DCs in cancer. Although we find this topic fascinating and believe it deserves discussion, we prefer to only discuss tumor-associated macrophages in the context of pancreatic cancer in this manuscript.

Reviewer #2:

This review appropriately includes references from both human and mouse studies. However, there are some important differences in the biology of human and mouse macrophages. As summarized by Schneemann and Schoeden in *J Leukoc Biol.* 2007 May;81(5):1334 (PMID: 17332373), human macrophages (in contrast to mouse macrophages) have neither NOS nor arginase activity. This species difference should be made clear to the readers. Furthermore, I would recommend separating mouse and human data in different paragraphs and discussing similarities and differences between the two species at the end.

We appreciate the reviewer's comment. We agree that there are important differences in the biology of human and mouse macrophages that must be delineated. Throughout our manuscript, we have attempted to clarify for the reader what species we are referring to so as to avoid confusion. Although separating mouse and human data into different paragraphs would avoid confusion on the readers' part, we believe that most of the data from mouse and human studies complement each other and provide for a better discussion if mentioned in the same paragraph.

On page 9, references should be provided after the sentence "However, in most tumors such as breast, prostate, ovarian, cervical, lung carcinoma, and cutaneous melanoma, TAMs are associated with a poor prognosis."

This sentence has been revised in the edited manuscript (page 8).