Reviewer's report

Title: Tumor associated macrophage-derived IL-6 and IL-8 enhanced invasion of LoVo cells induced by phosphatase of regenerating liver in a intermediate-conductance Ca2+-activated K+channels-dependent manner

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Reviewer: Lisha Kuang

Reviewer's report:

The manuscript concerns tumor associated macrophages facilitated PRL-3-induced invasion of LoVo cells. IL-6 and IL-8 secreted by TAMs, which are induced by KCNN4, play an important role in the functions.

It is very good to use different methods to verify the hypothesis. Especially, the result of patient specimens made the story more credible. I think that the rationale and logic of experimental approach are correct. The obtained results generally proved the hypothesis. However, the language in the manuscript needs to be improved. The title is too confusing to be understood. It is correct but difficult to figure out the meaning. Besides, some terms used in the manuscript are confusing too. For example, the “control-LoVo” in figure 2C needs to be redefined. To my understanding, the “control-LoVo” means “LoVowith low PRL-3 expression”. Is it correct?

Specific comments:

1. The authors concluded that TAMs participated in PRL-3-inducedmetastasis of CRCs through the TNF-#mediated secretion of IL-6 and IL-8. While the data did not show any change of TNF-#level in any cell type. The authors claimed that “Our previous research has found that PRL-3 could enhance metastasis of CRCs through up regulation of intermediate conductance Ca2+-activated K+ (KCNN4#channels which is depend on the autocrine secretion of TNF-#”, which is not convincing. The authors should show the expression or secretion level of TNF-# in PRL-3-LoVo, “control-LoVo”, control TAMs, knock down TAMs, and co-culture cells.

2. In Fig. 1, what is the role of this piece of data in the whole story? It needs to be clarified in the discussion section.

3. In Fig. 5, why did authors pay attention to the highest and third highest cytokine (IL6/IL8) but leave the second highest one (IL10) behind? It needs to be discussed more.

4. In Fig. 6C, it is not clear what “IL-6+ and IL-8+ TAMs” means. Does it mean “IL-6 positive TAMs and IL-8 positive TAMs” or “IL-6 and IL-8 double positive TAMs”? The authors should revise the description to make it easier to understand.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.