Reviewer's report

Title: Pancreatic adenocarcinoma exerts systemic effects on the peripheral blood myeloid and plasmacytoid dendritic cells: an indicator of disease severity?

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Reviewer: Paola Allavena

Reviewer's report:

The paper from Tjomsland et al. addresses the question whether patients with adenocarcinoma of the pancreas or other pancreatic diseases (including pancreatic tumors and pancreatitis) present a defect in circulating DC number or function. This impairment might represent a mechanism of immune evasion of the tumor.

Although the issue addressed by the Authors is very important in the cancer field and the work performed is based on an effort-consuming analysis of patient samples, the question posed by the Authors is not well defined: it's not clear whether the aim is to compare circulating DC numbers in a number of pancreatic tumors or to dissect the role of inflammation (since pancreatitis is included in the analysis) in the DC impairment observed. The overall conclusion is that it's not clear whether the DC impairment in tumor patients, which has already been described extensively in the literature, is something restricted to PDAC compared to other pancreatic tumors or to tumors compared to pancreatitis or is something observed in general in pancreatic pathologies.

Major Compulsory Revision:

1. The work is very defective in originality, being some of the data already reported in the literature, as the Authors themselves point out at the beginning of the 2nd and 3rd Result paragraphs. The previously undescribed finding that would have given some novelty to the present work would be here the extension of the analysis to other pancreatic tumor types; then, Authors should have made an effort to clarify whether the other pancreatic tumor types display differences compared to the adenocarcinoma. When they do observe a difference between PDAC and other tumors, (Figure 2), they do not discuss the finding.

2. Authors mention a population of non-DC cells which does not decline in tumor patients. They could have made an effort to better characterize this population (are they macrophages, neutrophils?). The availability of conjugated antibodies allows discriminating a lot of subsets, therefore defining a population as a "non-DC" does not sound appropriate.

3. A very important and missing point is the evaluation of DC numbers at the tumor site. The decrease in circulating DC number may just mirror a massive accumulation of these cells at the tumor site.

4. The analysis of the inflammatory mediators is patient plasma is very incomplete; for instance, CXCL8, her found increased in tumor patients, is a
chemokine, very important in neutrophil recruitment: this may imply a disregulation in neutrophil or monocyte blood count, that the Authors could have discussed.

5. An important point of the work is the recovery of DC number after surgery. Authors should have investigated whether those few patients showing total recovery in DC numbers had a different prognosis in terms of survival. This would confirm the importance of the DC number evaluation performed.

6. Authors often refer to impairment of DC functions in tumor patients, but their data is only based on number of cells and no report about function of DCs is present.

Minor essential revision:
1. 1st paragraph of results should better be included as a Method paragraph.
2. Figure 2: where is the plot of the control subject?

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

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