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: Peter S Goedegebuure

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Major Compulsory Revisions:
1. The authors do an excellent job of finding controls for this study encompassing multiple malignant diseases and a benign entity (CP), however there is little data in this paper which distinguishes a benign entity- CP- with a malignant one—PDAC. Additional experiments evaluating possible differences between the DC defects among CP versus PDAC patients should be performed to justify the proposed focus on “preservation of the blood DCs compartment in PDAC”.
2. While this paper presents an interesting idea and furthers information regarding subsets of DCs in patients with pancreatic cancer, but the authors provide a primarily descriptive paper with no mechanistic data. The finding that PGE2 and CXCL8 are upregulated along with apoptosis in DCs, as illustrated above would provide one area with which to further investigate this defect and provide mechanistic information. For example, is there a way to rescue these cells? Can PDCs and MDCs from normal controls be induced to become apoptotic by using culture medium from human pancreatic cancer cell lines, CXCL8, PGE2 or serum from cancer patients from this study? Are the DC from PDAC patients functionally different from those in CP or healthy donors?

Minor Essential Revisions:
1. Grammar and spelling throughout the manuscript should be checked: from the conclusion of the abstract “Our findings demonstrate the involvement of inflammation in the destruction of the blood DCs and that a preservation of the blood DCs compartment in the PDAC patients seems to benefit the patients ability to coop with the disease.”
2. In the Results section the authors delineate that the depression in PDCs and MDCs persists, and may be worse at 12 wks. Citation 26 showed restoration at 1 yr but also does not delineate a time course for resolution. A longer study time period with more time points would provide a framework for resolution of this defect and provide potential implications to the development of immune based treatment strategies.
3. In addition to the above, further time points reviewing defective antigen presentation and increased apoptosis would provide further insight into this defect.
4. The inclusion of the authors' data regarding PGE2 and CXCL8 is confusing as
they do not make a connection with the data regarding DCs in this study. There is evidence that PGE2 causes defective antigen presentation and defective crosstalk in vitro (Ahmadi M; Cancer Res, Sep 2008:7520-9), however there is no published data to suggest PGE2 increases apoptosis in DCs. Potentially the authors could look at PGE2 levels at each time point and elucidate if there is a connection between timing of PGE2 level normalization and DC reconstitution. Additionally, in vitro studies with PGE2 and DCs with apoptosis as the measurement would provide additional data and a potential mechanism for increased apoptosis in these cell populations.

Discretionary Revisions:

1. Figure 2B is an example of the flow completed for patients, however the gating is different in the two examples that are shown. From the figure it doesn’t appear as though it would change the percentages significantly if the gating was made uniform.

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

Declaration of competing interests:

I declare that I have no competing interests