**Reviewer’s report**

**Title:** Microparticles shed from multidrug resistant breast cancer cells provide a parallel survival pathway through immune evasion

**Version:** 0  **Date:** 20 Jul 2016

**Reviewer:** Sahil Mahajan

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The manuscript by Jaiswal R. et al investigated the effect of microparticles (MPs) isolated from drug sensitive and drug resistant human breast cancer cells as well as non-malignant cells on THP-1 derived macrophages. The authors observed that MPs derived from multidrug resistant (MDR) breast cancer cells modulates macrophage functionality by modulating cytokine secretion, by reducing chemotaxis and by inducing the engulfment of macrophages by MDR breast cancer cells. The authors also observed that MPs derived from MDR breast cancer cells induce aggregation of macrophages that involves HA mediated activation of CD44 on the surface of macrophages.

The findings shown in this manuscript are interesting as it highlights the intrinsic ability of MPs derived from drug resistant cancer cells to modulating macrophage function. However, certain points need to be addressed as outlined below:

**Specific comments:**

1) In figure 1, the authors should use FlowJo software (if available to them) to obtain their FACS plots in normalized to mode fashion.

2) In figure 2, 3, 4 and 5, the authors should mention in the figure legend the statistical test used to determine the significance.

3) In figure 2, it is quite unexpected to see that macrophages show change in the expression of IFN\(\gamma\) in response to MPs as IFN\(\gamma\) is a cytokine majorly produced by Th1 cells and not macrophages.

4) It might be interesting to use primary blood derived monocyte macrophages to validate some of the findings shown in the manuscript.

5) Conventionally, tumor cells induces M2-type TAMs in tumor infiltrating macrophages to promote immune escape for the tumor cells. But the findings shown in this manuscript
highlight the induction of M1 phenotype in macrophages in response to MPs. How the authors explain these unexpected results? Moreover, the authors should use more comprehensive profiling of macrophages before concluding that MPs induce M1 polarization of macrophages.

6) The discussion section is repetitive of results section and is too descriptive of the results obtained from this work. The discussion should focus on a more comprehensive review of the literature and hypothesis than an overview of the obtained results.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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