Reviewer's report

Title: Aspirin and P2Y12 inhibition attenuate platelet-induced ovarian cancer cell invasion

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Reviewer: Vahid Afshar

Reviewer's report:

In this manuscript, Cooke et al. reported the results of their studies on the interaction between platelets and two ovarian cancer cell lines (59M and SKOV3). The authors showed that platelets increase invasiveness of SKOV3 cells and alter gene expression pattern in these cells promoting EMT. Platelets did not alter invasiveness of 59M cells and induced less change in the EMT gene expression profile of these cells. Antiplatelet reagents 2MESAMP (P2Y12 inhibitor) and aspirin (COX1 inhibitor) reduced platelet-induced increase in invasiveness of SKOV3 cells.

Major Compulsory Revisions.

(1) One of the main conclusions of the study is that the interaction between different ovarian cancer cells and platelets is heterogeneous, as reflected in responses of different ovarian cancer cell lines after incubation with platelets. Authors should use more than 2 cell lines to demonstrate heterogeneity. Repeating invasion assays with additional ovarian cancer cell lines will support this conclusion.

(2) In figure 1A and 5A, platelet adhesion to cancer cells was measured by flow cytometry using anti-GPIb antibody. I assume that the authors used the size of particles to distinguish cancer cell/platelet clumps and platelets. How did the authors eliminate the possibility of counting platelet aggregates as cancer cell/platelet clumps? Usually to detect adhesion of platelets to cancer cells by flow cytometry, double staining protocols are used (one antibody against platelets and one against cancer cells).

(3) In the text and in the figure legend 5, authors mentioned that antiplatelet reagents did not affect the EMT gene expression profile in cancer cells, but the presented data in figures 5B and 5C showed that 2MeSAMP and aspirin changed the gene expression in these cells. Furthermore, if antiplatelet reagents did not change the platelet-induced EMT gene profile in cancer cells then how did they reduce invasiveness of cancer cells?

Minor Essential Revisions

(1) In the figure legend 3B, authors mentioned that the results expressed as fold change in mRNA expression. These results are not reflecting any change in gene expression but are the baseline mRNA expression profile of 59M and SKOV3 (in the absence of platelets).
(2) In the figure legends 2, 3, and 5, B2M should be spelled out at least once. Is it beta 2 microglobulin?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**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.