Reviewer's report

Title: Hypoxic enhancement of exosome release by breast cancer cells

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Reviewer: Wolfgang Mueller-Klieser

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Summary
In this in vitro study on three different breast cancer cell lines the release of exosomes was found to be enhanced by hypoxia. Analysis of exosomal constituents at the protein and RNA level resulted in the identification of elevated levels of the hypoxia-regulated micro-RNA miR-210 under hypoxic versus normoxic conditions. The authors conclude from their data that hypoxic cancer cells may promote their survival and invasion under hypoxia by enhancing exosomal release.

Major compulsory revision required (#1):
The release of exosomes by cancer cells and its regulation is an exciting novel field of cancer research. As such, the manuscript is addressing an actual and clinically relevant topic in the field. The concept of the study, however, is to some extent confusing with regard to its focus. It seems that the study was set up for demonstrating the superiority of a commercial assay for the isolation of exosomes from cultured cells as compared with conventional approaches. Provide that this was one goal of the study, and taking into consideration the high yield of exosomes obtained by the commercial technique of isolation, the poor quality of the immunoblots (Figs. 1D, 2B, and 3C,D) is surprising. It seems questionable whether this blots support the authors’ conclusions. Better original blots are required to be convincing with regard to the authors’ conclusions.

Major compulsory revision required (#2):
One further concern is the lack of novelty in the authors’ findings, as mirrored in their conclusions in the abstract and at the end of the discussion section. A hypoxia-induced increase in the release of exosomes by cancer cells has already been shown by the senior author and by others, as partially referenced in the manuscript (refs. 24 and 42; see also: Gutwein et al., 2005, or Ngora et al., 2012). It is not clear from reading the manuscript which novel knowledge is contributed to the field by the data presented. The authors need to reword their results, discussion and conclusion sections in order to precisely present what is new.

Level of interest: An article of limited interest

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