Reviewer's report

Title: MicroRNA in exosomes isolated directly from the liver circulation in patients with metastatic uveal melanoma

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Reviewer: Riccardo Alessandro

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The manuscript "MicroRNA in exosomes isolated directly from the liver circulation in patients with metastatic uveal melanoma" by Eldh et al. presents new data on the presence of exosomes into the liver circulation in patients with metastatic uveal melanoma. Authors found that exosomes from the liver circulation of affected patients are enriched in some microRNAs, thus suggesting their potential use as diagnostic markers.

The paper has a number of preliminary observations and the potential interest is hampered by some flaws mainly related to the paucity of samples. The paper can be considered for publication in BMC cancer pending the following revisions.

Major Points

1. For the clinical significance of the manuscript, it could be determinant to compare the miRNA profile of exosomes from metastatic patients with the miRNA profile of exosomes-derived from the peripheral blood of non-metastatic patients.

2. Authors presented data about the characterisation of exosomes from liver perfusate but the characterisation of peripheral blood-derived exosomes is missing.

Minor Points

1. In the discussion section authors should concentrate more on the discussion of the miRNAs that belong to cluster 3 that seems to be melanoma-specific.

2. line 236-239 (discussion section): authors say: Comparison of the exosomal miRNA profiles of patients and cell lines using cluster analysis revealed a clear relationship between the patient samples. Interestingly, the two melanoma cell lines did not cluster together, but did form a cluster together with the other cell lines”. Authors should discuss more this section. Why do they think that melanoma cells-derived exosomes have a microRNA profile more similar to other cancer cell lines (lung and breast) with respect to the exosomes isolated from the liver perfusion of metastatic uveal melanoma patients?

3. In material and method, line 103-104, authors say that “in addition to the liver perfusate, peripheral blood samples were taken prior to IHP and at 4 weeks, 3
months and 6-12 months after IHP”. In the results presented (fig. 3) they isolated exosomes from the peripheral blood prior to IHP showing data about the increase in circulating exosomes with respect to healthy control. No data are presented on exosomes isolated at other time points (4 week, 3 months, 6-12 months). What have been done with these samples? The analysis of extracellular vesicles before and after IHP could be significant.

4. line 299-300 (discussion section): authors say: “The analysis revealed multiple miRNA clusters, with cluster 1 and 2 (Figure 4C) being similar among patients and four of the five melanoma cell lines”. In the manuscript is written that the melanoma cell lines used for the experiments are 2: A357 and MML-1, while from the sentence it seems that authors have considered five melanoma cell lines. Please correct.

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

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests: NO