Peer Review File

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Reviewer A

Overall, the manuscript is well-written and broadly covers the clinically significant topic of Extracellular Vesicles (EVs) involvement in Prostate Cancer development, diagnosis and therapy. The manuscript is written according to guidelines for authors.

However, one of the concerns is that even thought the authors mention the ISEV recommendations for nomenclature and minimal information required for study description they do not provide informations whether the studies they mention throughout the manuscript comply with those requirements. It would highly increase the manuscript's value to provide the information on whether studies provided the information required for proper EVs identity and reproducibility, which is especially important in this confusing, demanding and rapidly developing field.

Reply: Thank you for your comment. According to the reviewer's comment, we added the following sentence in the revised manuscript "which will enable the creation of a review that is in accordance with the recommendations of the ISEV".

Change in the text: Page 7 103-104.

Reviewer B

1. Please describe relevant background, reasons for conducting this review, and <u>primary objectives of this review</u> in the "Background and Objective" section of the abstract.

Reply: Done.

- 2. Please re-organize the article following the Narrative Review guidelines. The attached checklist should be provided as an additional file. Reply: Done.
- 3. You refer to "studies" with only one literature citation several times. Please check and revise.

Reply: When only a single paper is cited, it is because it is a review article. As such, this paper encompasses a multitude of studies, thus making my statement accurate.

4. Please provide figure captions for subfigures 3A-3D and 4A-4C. Reply: Done

- 5. Abbreviation should be spelled out the first time it is used in the Abstract/Body Text/Figure/Table.
 Reply: Done.
- 6. The author's name cited in the text should be consistent with the reference. L1 might be a valuable therapeutic strategy (60). Lie et al. found that PD-L1 was transferred via EVs from PCa cells expressing high levels of PD-L1 to PCa cells expressing lower levels, thus aiding the ability of PCa to evade immune cells (61) modulating GREM2 expression via the TGF-β signaling pathway (47). Moskwa et al. showed that chemotherapy significantly upregulated miR-27a expression in PCa CAF. EVs from the PCa CAF were rich in miR-27a, which increased chemoresistance by targeting the gene encoding P53 (48). Additionally, Jiang et al. Reply: Done.
- 7. There are no labels (a), (b), and (c) in Figure 2.

 Figure 2. The roles played by EVs in the several phases of PCa progression. (a)

 Initiation, (b) localized PCa, and (c) metastatic PCa. EV: extracellular vesicles; CAF:

Reply: Done.