Reviewer 3: Minor revision

Dear Reviewer:

Thank you for your revisions and suggestions which add value to the manuscript. Please find below line by line answers to your queries (in blue). In the revised document, your revisions are highlighted in GREEN for your convenience.

The review by Dr. Vaiselbuh is dedicated to the role and diagnostic potential of exosomes in cancer. Exosomes are secreted, nano-sized vesicles that contain RNA species and proteins protected by a lipid bilayer containing specific transmembrane proteins. The biogenesis and role of exosomes in cancer is discussed. The largest part of the review is dedicated to the clinical utility of exosomes in cancer: its diagnostic and therapeutic potential. The figures and tables are very informative.

Minor Remarks

- P5: please update the online exocarta database with two new recent initiatives such as vesiclepedia and EVpedia
  

  Answer: Page 6, line 8: Reference # 39-41 added.

  In addition two new recent initiatives are free available online as reference databases for exosomes investigators: Vesiclepedia (a compendium for extracellular vesicles with continuous community annotation) (Kalra) and EVpedia ([http://evpedia.info](http://evpedia.info)) (an integrated database of high-throughput data for systemic analysis of extravesicular vesicles) (KimDK – Kim DK)

- p6: Schonnenschein should be Sonnenschein

  Answer: Change made: p.6: Sonnenschein
- Exosomes are difficult to discriminate from protein aggregates and lipoprotein complexes; especially if using complex biological matrices. A recent effort comparing different exosome isolation methods revealed a disparity in the yield and content of “exosomal” RNA. The results of this study clearly reveal that minimal experimental requirements are necessary to define exosomes. 
  

Answer: Page 11, bottom line: References # 84-86, 33 added.

A consensus need to be reach on dependable isolation methods for exosome biomarker research (Van der Meel). Reproducible protocols that obtain the purest exosome fractions for downstream RNA profiling with lack of contaminating Argo2-complexes would meet the standards of clinical care (Van Deun, Mestagh, Kalra 2013).

- figure 1
  
  why become the cells larger from top to bottom??

  Nucleus and endosome should have similar size in all cells. Is there evidence that MVBs in cancer cells are larger than MVBs in normal cells.

Answer: Corrections made : see Figure 1 in main doc.