Reviewer's report

Title: Extracellular vesicles: potential applications in cancer diagnosis, prognosis, and epidemiology

Version: 1 Date: 18 December 2014

Reviewer: Rui Henrique

Reviewer's report:

This review is focused on the role of extracellular vesicles in tumorigenesis and on how this knowledge may provide relevant information and tools for cancer patients' management.

Despite the wealth of existing information on this subject, the manuscript is rather short and it is not always apparent why certain data is mentioned and other is not.

Along the text there is sometimes a lack of clarity as well as the repetition of ideas (e.g., the potential epidemiological impact of EV which is referred to several times).

Language could be refined to provide a more dynamic text with a better connection between sentences and statements.

Major compulsory revisions
- The section on EV biogenesis would benefit from a more detailed and updated description of the process, the mechanisms involved and the main players.
- In the EV functions, there is a lack of information concerning the genomic DNA content. Some recent studies using NGS found that double-stranded genomic DNA spanning all chromosomes may be detected in the serum exosomes of patients with pancreatic cancer (Kahlert et al., 2014). This type of information must be included.
- The section on methodology for isolation and analysis of EV will benefit from the inclusion of a Table summarizing the most relevant of those issues. More updated references should be used.
- The section on the pathological functions of EVs seems to be misplaced as it would sound more rational to place it before the use of EVs in diagnosis.
- The first paragraph in page 10 does not seem to belong to a section on therapeutic purposes and should be re-allocated to another section.
- There are many references which are themselves reviews on the subject or related subjects. Although this contributes to the economy of the text, it fails to provide the most important and higher impact references in the field which are the original reports.
- In Figure 1 legend, it is stated that exosomes may also be formed directly from
the cell membrane. This is not stated in the text (namely on page 3, line 10). Moreover, no reference is provided for this statement.

Minor essential revisions
- Page 3, line 7, should read "endolysosomal"
- Page 5, line 13: please replace "lung pleural effusion" by "pleural effusion due to lung cancer"
- Page 9, line 9, should read "neoplastic cell-to-normal cell"
- Page 12, line 2, should read "providing"
- In Table 1, in several places, it should read "was conducted on"

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

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