Reviewer's report

Title: A Mouse Model for Triple-negative Breast Cancer Stem Cells (TNBC-CSC) Exhibits an Aggressive Phenotype

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Reviewer: Jin-Qiang Chen

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In this manuscript, authored reported the development and molecular/pathological characterization of a new stable triple negative breast cancer (TNBC) cell model. They transfected 4T1 cells, a highly metastatic breast cancer cell line derived from a spontaneously arising BALB/c mammary tumor, with rat ER, PR and HER2 and then sorted for cells with high expression of these proteins by flow cytometry and examined their expression levels by Western blot. More interestingly, they further produced TNBC-cancer stem cells (TNBC-CSC) and TPBC-CSC by sorting CD24+/ALDH-1+/CD44high expressing cells from TNBC and TPBC. and observed that implantation of these TNBC-CSC into naïve female BALB/c mice resulted in significantly larger tumors with significantly higher metastatic potential to the lung. An increased aggressiveness of TNBC-CSC correlated with increased expression of Hesp25 and Hsp72, which have been shown to promote the progression to more malignant phenotypes and are related to higher metastatic potential. This newly developed TNBC cell models could be useful tool for the studies on the pathogenesis and therapeutic treatment for TNBC.

This study addressed a critical need in TNBC research, i.e. TNBC cell model and is quite important and interesting in the field of TNBC. The methods used in this study were appropriate and the data were clearly presented and solid. The manuscript was concise and well written. The introduction was well organized and informative. The discussion addressed the important points which were well supported by the data. However, the limitations of this work and how the model is appropriate for TNBC research need to be further addressed as well.

There are several abbreviations that need to be defined when they first appear. For example, ALDH1 in page 9 and several more in other pages. Please check throughout the text to make corresponding changes.

Level of interest: An article of importance in its field

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'