Reviewer’s report

Title: Macrophage traits in cancer cells are induced by macrophage-cancer cell fusion and cannot be explained by cellular interaction

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Reviewer: Lill-Tove Busund

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Macrophage-specific antigen CD163 expression in tumor cells has been reported in several cancers and proposed being caused by macrophages-cancer cell fusion rather than by paracrine cellular interaction in tumor stroma. This study examines the cell fusion process as a biological explanation for macrophage phenotype and provides new insights into the role of cell fusion.

Monocytes activated to M2 macrophages and co-cultured in a transwell system with cancer cells generated phenotypical and functional cancer cell-macrophage hybrids by spontaneous cell fusion. The in vitro studies seems convincing with strictly defined experiments.

Major Compulsory Revisions

The manuscript needs major revisions on the human cancer examinations. The IHC staining of CD163 expression in breast tumor samples from women by immunohistochemistry (IHC) should be performed by double IHC: this enable the authors to visualize the CD163 (macrophages) and cytokeratin (cancer cells) in one and the same cell. Expression of only CD163 + cells in neoplastic cell compartments of the tumor does not prove cell fusion, but rather infiltration of CD163 + cells in the cancer cell areas.

Magnification of the histological pictures should be stated (in bars).

Figure 5a, upper picture: The blue arrow points to lymphoid cells in tumor stroma. The lower picture shows a lot of macrophages in tumor stroma and some inbetween the neoplastic cell population.

Minor Essential Revisions

Some abbreviations should be explained, like GFP etc.

The concentrations and type of the antibodies and the isotype controls should be stated in the M&M section.

Table I should be replaced by a venn diagram.

For how many weeks were the hybrids cultivated? Did they keep the same phenotype and functionality over time?
Level of interest: An article whose findings are important to those with closely related research interests

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

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests' below.