Reviewer's report

Title: The endogenous soluble VEGF Receptor-2 isoform suppresses lymph node and lung metastases in a mouse immunocompetent mammary cancer model

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Reviewer: Norihiko Tsuchiya

Reviewer's report:

The authors investigated the effects of endogenous soluble VEGFR2 gene therapy on murine mammary cancer model. The data mainly led by histological observation demonstrated that esVEGFR2 receptor gene therapy inhibited both distant and lymph node metastases, suggesting the possible application to the treatment of metastatic breast cancer. It is also very interesting that esVEGFR2 inhibited the tumor growth without suppression of tumor neovascularization. This study is well-written and interesting from the view point of esVEGFR2 function in cancer growth and metastasis.

Major Compulsory Revisions:

1) The authors hypothesized that growth and metastasis of BJMC3879 cells were modulated by VEGF-C through its receptors VEGFR2 and/or VEGFR3. How is the expression status of VEGF-C, VEGFR2, and VEGFR3 in BJMC3879 cells?

2) Were esVEGFR2 and endostatin expression levels or fold changes confirmed after the gene transfection?

3) Although metastases were observed in lymph nodes, lung, kidneys, adrenals, and uterus, some mice had metastases in over 10 organs according to table 1. How was the number of metastatic organs counted?

4) The counting methods of TUNNEL-positive cells and BrdU-positive cells were precisely described in the text. How was the number of blood vessels, lymphatic vessels, and lymphatic vessels with cancer cells counted?

Minor Essential Revisions:

“psVEGFR-2” in figure 1 and 3 should be replaced by “pesVEGFR-2” as described in the text.

Which journal?: Not appropriate for BMC Medicine: an article of only archival interest, but might be suited to BMC Cancer

What next?: Offer publication in BMC Cancer after discretionary revisions

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