Reviewer’s report

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

Version: 2 Date: 5 October 2010

Reviewer: Bronislaw Pytowski

Reviewer’s report:

I am basically satisfied with the replies to my review and changes in the manuscript. However, some of the changes made contain major grammatical errors that should be carefully corrected. Most of the red text should be carefully edited. I provide some examples below:

Page 5: "In addition, since endostatin is also naturally occurring molecule and exerts both inhibitions of blood and lymphatic vessels, this gene was served as a positive control [15, 16]." change to "...this protein served...

Pages 12 and 13: "Inhibition of lymph node metastasis in the pEndo group (positive control) showed significantly stronger than in those observed in the pesVEGFR-2 group (Fig.3A): change to "......(positive control)WAS significantly..."

Page 15: "Although the inhibition of metastasis in these groups may simply be a reflection of suppression of tumor growth and decreased cell proliferation, this therapeutic benefit is apparent because patients presenting metastatic disease are frequently incurable using conventional therapies." This sentence needs to be divided in two. First, discuss the experimental results. Then, speculate on correlation with human disease. As is, the sentence is very difficult to understand.

Page 15: "Thus, pesVEGFR-2 therapy that offer the prolonged survival, the reduction in tumor volume and suppression of metastasis have significant clinical implications." I am not sure what the authors are trying to say. Please rephrase. For example (if authors agree): "Prolonged survival, reduction in tumor volume and supression of metastasis after pesVEGFR-2 therapy suggest that sVEGFR-2 may potentially represent a novel therapeutic for cancer treatment"

Page 16: Most of the red section should be carefully rewritten. For example: "...it may be associated with non-effective for angiogenesis by pesVEGFR-2." may be changed to :...treatment with pesVEGFR-2 that primarily inhibits lymphangiogenesis may be ineffective in this experimental setting."

Page 17: "...However, since anti-VEGFR-3 antibody also acts as trap for VEGF-C [2, 31, 34], further investigation is necessary to elucidate this point." This needs to be changed. Anti-VEGFR-3 antibodies do NOT act as VEGF-C traps. This only
happens with soluble receptor or antibodies to VEGF-C.

Page 18: "Brideau et al. reported that J4 transgenic mice overexpressing endostatin in the epidermal basal cells inhibit both angiogenesis and lymphangiogenesis in skin tumors induced by a carcinogen followed by a promoter [16]." change to something like "...Brideau et al. reported that in J4 transgenic mice in which overexpression of endostatin in the epidermal cells is driven by (which promoter? Keratin?) both angiogenesis and lymphangiogenesis were inhibited in skin tumors induced by a carcinogen"

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 am an employee of ImClone Systems, a wholly owned subsidiary of Eli Lilly and Company. Some of my work relates to therapeutics that target VEGF receptors 2 and 3.