Title: Cell type- and Tumor zone-specific expression of pVEGFR-1 and its Ligands influence Colon cancer Metastasis

Version: 2
Date: 2 December 2014

Reviewer: Margaret Currie

Reviewer's report:

Cell type- and Tumor zone-specific expression of pVEGFR-1 and its Ligands influence Colon cancer Metastasis.

Caren Jayasinghe, Nektaria Simiantonaki, Charles J Kirkpatrick.

This manuscript describes immunohistochemical analysis of VEGFR1 and its ligands by tumor compartment and cellular location in colorectal cancer samples. The research question posed by the authors is clearly defined, the methods are appropriate and well described, and the data is sound. Overall, the paper is well written and is a coherent and sound addition to scientific knowledge in the area. However, the discussion is overlong, and contains no discussion of the limitations of the study.

Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures or the wrong use of a term which the author can be trusted to correct)

Background

Spelling ‘Background’ title.

Paragraph 6 (and throughout manuscript). Include published reference for (Jayasinghe et al, submitted), or refer to ‘own unpublished data’.

Methods and Materials

Paragraph 3. Can the authors clarify ‘vegetable steamer’? Is it the same as a ‘pressure cooker’ used in Paragraph 4? How could others replicate this method?

Discussion

Paragraph 7. Change ‘In light of these controversial data’ to ‘In the light of these contrasting findings’.

Table 1. Why is VEGF-B score cut-point different in tumor center and tumor budding? Be consistent with use of VEGF (in text) and VEGF-A (in tables).

Figures 1 and 2. Remove the continuous red, blue and green lines between percentage points in Zones 1, 2 and 3. These are discreet tissue areas, and not
continuous measurements.

Figure 5. How is VEGFB promoting metastasis in tumor cells in the tumor center and in extratumoral small vessels?

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

Background
Paragraph 4. Replace ‘controversially discussed’ with ‘remains controversial’.

Methods and Materials
Paragraph 1. Consider changing to ‘Written informed consent was obtained from all patients’.

Paragraph 3 and 4. Consider changing ‘provider’s instructions’ to ‘manufacturer’s instructions’.

Results
Paragraph 1. Consider removing sentences 5 and 6 to discussion.

Table 1, 2, 4, 5 & 7. Delete ‘and/as well as statistical significance’ from table titles.

Minor Issues - Not for publication

Background
Paragraph 5. VEGF-B, another ligand of VEGFR-1, seems to be…

Results
Paragraph 3. Delete ‘enough’ from ‘Interestingly enough’.

Paragraph 10? (Figure 4 and 3E).

Figure 5 legend. Insert space ‘(zone2)’.

Level of interest: An article of importance in its field

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.