Reviewer's report

Title: Coexpression of VEGF-C and cyclooxygenase-2 and its Association With Lymphangiogenesis in Human Breast Cancer

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Reviewer: Kenichi Sugihara

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General
This paper studied about relationship among VEGF-C and COX-2 expression, lymph vessel density and clinicopathological findings of breast cancers.
The authors should describe how the histopathological examination was done.
The survival curves should show the sensors

(1) p4, Evaluation of Staining. Authors classified the intensity of COX-2 and VEGF-C expression only by the percentage of positively stained cells. Author should describe how the cells with moderate expression of COX-2 or VEGF-C (expression intensity was between positive control and negative control) were dealt with. Some authors classified COX-2 expression level by scoring method, in which both expression intensity of cancer cells and positivity rate (percentage of positively stained cells) are taking into consideration.

(2) p9, Discussion, the 3rd paragraph, the 2nd line from the bottom. Although the reference 21, a similar study, showed different result by studying VEGF-C in human breast cancer, authors of the present study commented only "the difference is due to the use of different antibody". Author should discuss much more deeply about the cause of their different results (number of the cases, patient's background, evaluation method of immunohistochemistry, statistical analysis, and so on) in detail.

(3) p2, Introduction, first paragraph the first line. Authors commented "spread of tumor cells by lymphatic vessels to regional lymph node is the initial step of further dissemination and....", which is not always true.

(4) p8, Result, the last paragraph, the 4th line from the top of the page. Authors should show a hazard ratio and P value of COX-2 and VEGF-C expression by multivariate analysis, even if the differences are not statistically different.

(5) p8, Discussion, the first paragraph, the 9th line. It can not be suggested by showing only the positive correlation between COX-2 and VEGF-C expression that COX-2 regulated lymph angiogenesis. If the relationship between COX-2 and VEGF-C expression has already shown in some basic researches (DNA transfecting study, etc), the document has to be included in the Reference.

(6) p10, Discussion, the 4th paragraph, the 10th line from the bottom. Did authors find the different expression level of COX-2 and VEGF-C among cancer cell, stroma cell and normal cell in this study? It is better to comment about the difference, if authors explain the differences of the result between the data by RT-PCR assay (Ref24) and the present study.

(7) p11, Discussion, the last paragraph. It is a considerable speculation that a COX-2 inhibitor prevents lymph node metastasis of breast cancer in clinical use.

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

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.