Reviewer's report

Title: The association between RCAS1 expression in laryngeal and pharyngeal cancer and its healthy stroma with cancer relapse

Version: 1 Date: 21 November 2008

Reviewer: Kenzo Sonoda

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Comments:

The authors immunohistochemically investigated RCAS1 expression not only in pharyngeal and laryngeal cancer but also in its clear surgical margin in order to evaluate an involvement of RCAS1 in local cancer recurrence. RCAS1 was identified in all cancer tissues. Moreover, RCAS1 was detected even in clear surgical margin samples at lower level than cancer. Intriguingly, RCAS1 expression was significantly strong in clear surgical margins in case of cancer relapse. The authors concluded that immune cell suppression connecting with tumor RCAS1 expression might be important for cancer recurrence. So far, there was no report regarding RCAS1 expression in surgical margins, making the results of this work valuable. However some suggestions are made below to be criticized:

(Major Compulsory Revisions)

1. In “Results” section, the authors described that “RCAS1 presence was also revealed in immunohistochemistry in all (96.5%) samples derived from histopathologically negative surgical margins” (page 9, line 15). However, RCAS1 is positive in 96.5% (50 positive cases in 51 total cases) in Table 2. Additionally, Fig. 3 shows RCAS1 immunoreactivity in cancer but not in clear surgical margins. The authors should revise the text in order to make readers understand clearly.

2. In “Results” section, the authors did not mention Fig. 4 and 5. The authors should describe the significance shown by these figures.

3. In “Methods” section, the authors described that 20 tissue samples were also obtained from the healthy mucous membranes of patients without cancerous lesions. However, there was no result concerning these healthy tissues. The authors should add data by using healthy tissues.

4. The authors discussed that RCAS1 expression in clear margins may contribute for cancer relapse, therefore I would suggest a consideration to characterize RCAS1 positive cells in order to understand biological significance of RCAS1.

5. The authors described that RCAS1 stromal expression might be responsible
for tumor invasion (page 12, line 8-11). However, RCAS1 expression was evaluated in cancer cells but not in stroma of uterine cervix (Sonoda K et al. Gynecol Oncol 2005; 99: 189-198). The authors should revise the text correctly.

(Minor Essential Revisions)
1. In “Methods” section, several typographical errors (for examples, 50I1/4g; I1/4m, etc.) should be corrected (page 6-7).

2. In Table 1, the numbers were indicated for positive lymph node metastasis with or without extracapsular spread. However, these numbers do not sum to 27. The author should correct numbers.

3. In Table 1, the numbers were indicated for tumor size, however, these numbers do not sum to 51. The author should correct numbers.

4. In Table 2, the authors should indicate an asterisk which was described in a footnote.

5. In Table 2, “in six specimens (20%)” should be corrected to “in six specimens (12%)” (line 1 in a footnote).

6. In Tables, the word indicating statistical difference “p” should be written as “P” (italic capital).

(Discretionary Revisions)
No suggestions.

That is all.

Level of interest: An article of importance in its field

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.