Reviewer's report

Title: Ep-ICD subcellular localization index (ESLI) is a novel marker for metastatic papillary thyroid microcarcinoma

Version: 1 Date: 2 August 2012

Reviewer: Sara Simonetti

Reviewer's report:

This is a very interesting article because at the moment knowledge on PTMC behaviour is still scanty. Therefore the present paper gives some new data interesting to better understand this type of tumour. Nevertheless several points should be clarified before publication.

Major Compulsory Revisions

1. The authors study 34 patients and they report the results of IHC expression of EpEx, Ep-ICD and ELSI in 2 separated group of tumors, metastatic and non-metastatic. Moreover they say, in the abstract and in the methods, that this separation of patients was based on the development of metastasis at diagnosis or during follow-up. In the results the authors report the differences of IHC expression of EpEx, Ep-ICD and ELSI in the 2 groups of patients, but they do not correlate this expression with the outcome of the patients. It could be very interesting to explain which is the outcome of the patients (reccurence or not) and which is the immunohistochemical behaviour of EpEx, Ep-ICD and ELSI correlating to the follow-up of the patients.

   The authors should introduce the follow-up data in the paragraph "Patient and Material" of the Methods; should add in the Results which is the correlation of IHC expression of EpEx, Ep-ICD and ELSI and the follow-up of the patients, also in a table, and should report in the Discussion their data.

Minor Essential Revisions

1. Title: The title should contain a reference to the used technique in the article. For example "Immunohistochemical expression of Ep-ICD subcellular localization index (ESLI) as a novel marker for metastatic papillary thyroid microcarcinoma".

2. Methods:

   - In the paragraph "Immunohistochemistry for EpEx and Ep-ICD expression in PTMCs" it is not reported which kind of counterstaining was used and which tissues have been used a negative and positive control of IHC technique.

   - In the paragraph "Evaluation of immunohistochemical staining" a reference of the validation of the applied score is not reported.

   - The title of the paragraph "Ep-ICD Subcellular Localization Index (ESLI)" is in bold and not subtitled as the others.

   - In the paragraph "Ep-ICD Subcellular Localization Index (ESLI)" a reference of
the validation of the applied score should be reported.

3. Results:
   - The authors should add a title to the first paragraph, for example "Patients".

4. Discussion: In the second paragraph "Current AJCC TNM staging recommends using a select few clinicopathological......" the authors should introduce a reference for this data and explain the significance of acronyms AJCC.

5. Figure 1:
   - D) The authors report the image as a metastatic PTMC showing strong nuclear and cytoplasmic Ep-ICD accumulation, but this image shows just a cytoplasmic distribution of the protein and not a nuclear one. The authors should modify the figure with a nucleo-cytoplasmic positivity of the protein.

6. Table 1:
   - In the first line "Gender" how many male patients are included in the study is not reported.
   - In the first column "Metastatic" the percentage in parentheses is omitted.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**
I declare that I have no competing interests