Reviewer's report

Title: PADI4 Has Increased Expression In Blood and Tissues of Malignant Tumors

Version: 1 Date: 2 September 2008

Reviewer: Lorne Hofseth

Reviewer's report:

The authors present comprehensive observational data indicating that PADI4 and/or citrullinated antithrombin levels are elevated in malignant tumors, and in the blood of patients with malignant tumors. Although this reviewer appreciates the amount of work that has gone into such a study, I have the following comments that need to be addressed:

Major compulsory revisions:

1. State the criteria for positivity in immunohistochemistry (IHC). This needs to be explained.

2. What are the positive and negative controls used for IHC results?

3. All IHC should be more quantitative. A good reference to use, if the authors don’t have an automated IHC quantification system is ‘Denkert C, Koch I, von Keyserlingk N, et al. Expression of the ELAV-like protein HuR in human colon cancer: association with tumor stage and cyclooxygenase-2. Mod. Pathol. 2006;9:1261-9.’

4. Because points 1, 2 and 3 above were not done, this reviewer disagrees with some interpretation of IHC. Only a few examples are that the authors state (page 10) that no significant immunosignals for PADI4 were detected in various benign tumors, including leiomyoma of the stomach, myoma of the uterus, endometrial hyperplasia of the uterus…'

The first issue is to define ‘significant immunosignals’. The second issue, here, is that if one takes a close look at Figure 1, there are clearly signals in all of the above named tissues (leiomyoma of the stomach, myoma of the uterus, endometrial hyperplasia of the uterus)

5. Because of the lack of quantification, to convince the reader/reviewer, the authors should also take a low power and high power magnification of each tissue they quantified. Add the pictures to supplementary data.

6. Figure 3: Standard Error bars are shown, but there are no statistics to indicate where significance is.

7. Figure 4: There are no Standard Error bars shown. I would envision there are standard errors with the numbers the authors indicate.
8. Figure 4: What is at the bottom of the figure?

Minor essential revisions:

1. ‘Benignant and/or benignancies’: this word is not usually used in a medical context. I think the authors mean ‘Benign’. Please change at appropriate places.

2. Abstract: 6th line down: change ‘…blood of many malignant tumors as compared with chronic…’ to ‘…blood of many patients with malignant tumors as compared to patients with chronic…’

3. Introduction: 3rd line from the bottom: change ‘…leukemia cells.’ To ‘…leukemia cells, respectively.’

**Level of interest:** An article whose findings are important to those with closely related research interests

**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