Author's response to reviews

**Title:** Increased PADI4 expression in blood and tissues of patients with malignant tumors

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**Version:** 3  **Date:** 21 December 2008

**Author's response to reviews:** see over
Dear editor:

We really appreciate comment and suggestion of editor and Dr. Badve and Dr. Lorne Hofseth. As we understand, Dr. Lorne Hofseth is satisfied with our response (see comment sheet 3849027302356117). In this resubmission, we corrected our mistakes and made modification based on suggestion of Dr. Badve. In fact, there are only point 1, 2 and 3 in the prior review. Space for point #4 is blank and has not any content on the comment sheet (see http://www.biomedcentral.com/imedia/1711597337226725_comment.pdf). So, we hope to get another chance from editor, if our revision is still not satisfied this time. In addition, we completely agree the point of view about expressions and roles of keratin in tumor tissues. We had made modification on discussion section in the prior resubmission. In the new resubmission, we addressed this point and cited view of this reviewer in the revised manuscript. If reviewers are still not satisfied with immunohistochemical results of chondroma and nevus, we plan to remove this part. Anyway, please give us a chance to introduce our results to other research in this area.

If editors and reviewers are still not satisfied with our revision, please let us known immediately and we will make further correction with our submission.

We would be very grateful if our submission is accepted by BMC cancer.

With best wishes,

Merry Christmas!

Xiaotian Chang
Respond to review of Dr. Sunil Badve

We really appreciate comment and suggestion of Dr. Badve. Based on his instruction, we corrected our submission as following:

1. “The authors have not addressed point #4 in the prior review. The photograph entitled chondroma does not contain cartilage but depicts bone marrow. Similarly the Nevus shows only skin, nevus cells are not present. The authors need to contact/consult a surgical pathologist.”

We really appreciate this reviewer. He found a big mistake we made in our submission.

In the prior review, there are only point 1, 2 and 3. Point #4 is blank and has not any content on the comment sheet (see http://www.biomedcentral.com/imedia/1711597337226725_comment.pdf). So, we did not immediately give response to the suggestion of point 4. To prepare this resubmission, we commercially obtained 50 tissue slides of chondroma and 80 tissue slides of skin cancer which were identified by surgical pathologists and pathologists of the manufacturer. In this revised submission, we selected new photographs of chondroma and nevus to replace old ones in Figure 1. In these new photos, we presented chondroma with cartilage and skin with nevus cells. As we reported in prior submission, PADI4 was significantly detected in tumors of chondroma and was not detected in nevus cells of skin tissues. PADI4 was expressed in intradermal nevus. The brown color is pigment in nevus cells. The color was also observable in the control
sections without 1st or 2nd antibody, indicating that the “signals” were not true immunosignals and caused by pigment.

2. “Modifications of Keratin profile occurs in cancer and can be used for diagnostic purposes- this does not mean that Keratin is a tumor marker. The reference cited in the cover letter is meaningless in this regard. All epithelial cells have keratin”.

   We completely agree this point of view. Keratin is not tumor marker, because the protein is also expressed in epithelial cells, although modification of keratin occurs in cancer. In fact, we had accepted suggestion of this reviewer and made correction in the prior resubmission. In this resubmission, we addressed this point and put view of this reviewer into the revised manuscript.