Author's response to reviews

Title: Stem cell abundant protein Nanog, Nucleostemin and Musashi1 highly expressed in malignant cervical epithelial cells

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Author's response to reviews: see over
Dear Editor:

We have revised our paper according to the reviewers’ comments, and invited the “International Science Editing” system to edit our English. The details are listed as followings. If you have any questions, please contact with me anytime.

Sincerely yours,

Best wish to you in Chinese Spring Festival

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Reviewer1:

Q1. The paper would benefit from being re-written with good english.
A: We have invited

Q2. There is no statement on the consent of patients.
A: We have obtained the consent of the patients and the approval of the Ethics Committee before the study began, it is our carelessness not mentioned this important problem in the first format; we have added it in the Page 4, lane 2.

Q3. The author said the semiquantitative scoring system was based on the percentage of positive cells and the stain intensity. However, there was no description on intensity explaining -(0) ~ +++(3). In addition, the agreement between the 2 pathologists should be presented.
A: We have detailed description on intensity explaining -(0) ~ +++(3); and the agreement between the 2 pathologists have been presented either in the Page 5, paragraph 2, lane 4 to lane7.

Q4. The staining sites should be presented (cytoplasm or nucleus) in the text.
A: We added the staining sites of the three proteins in the text at the end of the first paragraph of the result part in page5.

Q5. In a report [Sandro et al. Am J Surg Pathol 2006;30:1613], Nanog showed nuclear staining. The author should describe more detail about this.
A: Actually there was some reports indicated that Nanog is nuclear staining, we have paid attention to this question. In the study procession, we repeated the experiment by kinds of methods and designation, excluded the false positive staining, the Nanog protein was staining in the cytoplasm consistently. The mechanism was not clear till now, maybe need penetrating study in the future. We discussed this question in the 4th paragraph of Discussion in Page7.
Q6: In Figure 1, D showed membranous staining, which differ from that of B and C. What is the reason?
A: In Fig1 D, it is cytoplasm staining, but for the tumor cell dyskaryosis, the cytoplasm was squeezed close to the membranous looks like membranous.

Q7: Are there any correlations between the expressions of the three proteins?
A: There is high level expression of Nanog, Nucleosteimin and Musashi1 in embyro cells, indicated the cell differentiation, proliferation and division in the procession of embyro development. We chose these three typical molecule to reflect that the cervical carcinoma cells are a crowd of primitive cells.

Q8: Table 1 would be benefitted, if also presented as figures.
A: For the data shown in Table1 were rank data, it is too complicated to presented as figures, so we still remain this table in our paper.

Q9: Advanced stage tumors were not included in the analysis of Table 2. The different expression between early stage tumor and advanced stage will have much more information. In addition, how was the recurrence and its correlation with the expressions.
A: For the patients under surgical in our hospital were all early stage cervical carcinoma, we could not obtain the clinical-pathological prognostic factors of advanced stage patients, we could not analyze the relationship between the expression of these three protein and the clinical-pathological prognostic factors.

Q10: There is no correlation between the expression of stem cell abundant proteins and differentiation of tumor in table 2. Can the author explain the reason.
A: The “differentiation” in Table 2 was a concept in histology, and the “differentiation” in stem cells was a concept in cytological, there may be non-statistical different in the results.
Reviewer2:

Q1: The manuscript needs improvement in the quality of written English
A: The same to the Reviewer1’s Q1

Q2: The authors have chosen to look into detail at early stage cxca. I would propose to compare the early stage group as one group with the CIN ptn (as already done) and with more advanced cxca ptn. The result described in table 2 (with no significant differences except one could be predicted). A comparison between early stage and late stage cxca is more sound (and logical). It would be of value if the late stage ptn group could be extended.
A: As our answer to the Reviewer 1 Question 9, for the patients under surgical in our hospital were all early stage cervical carcinoma, we have only a few advanced stage patients and have no integrity clinical pathological data for these patients, it is difficult to study including the advanced stage patients or compare them as one group.

Q3: Result section in the abstract should contain more detailed information
A: We have detailed the result section in the abstract in Page 1, lane 2.

Q4: Background is not convincing. Why should I be interested in these 3 proteins in cxca ptns?
A: We have enriched the background section in Page 3 from lane3 to lane 6, and simplified the discussion part according the Q6.

Q5: Table 2 is of no value and can be left out. It can be described in the text.
A: Table 2 was deleted, we described the statistic results in the result section Paragraph 3.

Q6: In comparison to the results part is the discussion part to long. The role of the 3 proteins within embryonic development is to long. Within the discussion part I should be convinced why these 3 proteins are worthwhile to look at and what others already
published within the field of oncology. Furthermore a broader perspective should be
given why it is interesting to study these kind of proteins within CIN and cxca ptn.
A: We have simplified the discussion part as the reviewer’s advice, and added some
broader perspective for theses three protein in the clinical use in cervical carcinoma
prevention and treatment at the end of the discussion section.