Author's response to reviews

Title: Expression of Cyclooxygenase-2 and B-cell lymphoma-2 in cystitis glandularis and primary vesical adenocarcinoma

Authors:

Zhongxing Li (wxd0422@163.com)
Guangcheng Ge (315839923@qq.com)
Rui Feng (970286944@qq.com)
Dan Wu (chao8746@126.com)
Bin Shen (drxbju@gmail.com)
Xing Wang (707035180@qq.com)
Yan Cui (amyyicss@sina.com)
Junrong Li (452478970@qq.com)
Xiaobing Ju (doctorjxb73@njmu.edu.cn)

Version: 3 Date: 27 October 2013

Author's response to reviews: see over
Dear Dr. Philippe Spiess

Thank you for your email correspondence on 1-Oct-2013, in which you encouraged us to revise our manuscript (MS: 1288440221101870) entitled “Expression of Cyclooxygenase-2 and B-cell lymphoma-2 in cystitis glandularis and primary vesical adenocarcinoma”.

Based on your suggestions, we carefully studied the comments made by two professional reviewers. And then responded their questions. In addition, we asked a native speaker to help with the revision of this manuscript especially for the language improvement. Now you will see a revised (highlighted) manuscript attached as a main document. Below, you will find the point-to-point answers or clarifications to reviewers. In the end, We would like to thank the editor and the reviewers for their valuable comments and recommendations that have greatly improved the quality of this paper. We hope our responses are satisfactory.

Sincerely,

Xiaobing Ju, MD
Department of Urology
The First Affiliated Hospital of Nanjing Medical University
300 Guangzhou Road, Nanjing 210029, China
Tel: +86 25 83780079
Fax: +86 25 83780079
16-Oct 2013
Reviewer 1

1. **Were there any stains performed for CDX2 or CK7 two markers already evaluated in CG? It would be interesting to compare the findings of COX to CDX2 and CK7.**

A: Thank you for your asking, by reviewing the literatures, we found that both CDX2 and CK7 have been evaluated before, some studies suggested the CK7 were expressed in all CG cases collected with a mean percentage of positively staining cells of 63% [1]. One center demonstrated that the higher mRNA levels of CDX2 was detected in intestinal cystitis glandularis compared to typical cystitis glandularis (p<0.001) [2]. As for previous findings of CDX2 and CK7, we did not perform these two markers on CG.

2. **The current study has not demonstrated enough evidence to link the causality between COX-2 expression and "tumor initiation" - this language is too strong.**

A: I agree. We have changed this expression.

3. **The ADC groups are heterogenous - mechanisms of ADC in this group. Adenocarcinoma of the bladder can be one of many types including enteric, mucinous or signet ring cell. These should be differentiated. How old were each of these patients at diagnosis - primary exstrophy represents a very distinct population.**

A: Thank you for your suggestion. In this study, we failed to differentiate ADC group because the we focus on the CG instead of ADC, the ADC was just regarded as a positive control. Besides, some pathology reports of these 4 patients lack the exact cell types because of the early decade of diagnosis. We could check up these patients age by reviewing the case history, and their age at diagnosis were 66,72,52,and 59.

Reference


Reviewer 2

1. **In abstract, methods section:**
   a. please complete the sentence that this is a retrospective study.
   
   Page 4
   
   line 2- change CG was to CG is
   
   line 11- please change adenocarcinomatous to adenocarcinoma.
   
   line 12- change carcinoma to adenocarcinoma
   
   Page 6
   
   Line 17- remove ?

   A: I agree. We have changed all expressions pointed above.

2. **Major revision:**
Page 7

line 6- please describe in detail how the analysis is done using SPSS.
A: Mann-Whitney Test (Wilcoxon Rank Sum Test) basic procedures in SPSS: Select Analyze and Nonparametric Test, then independent samples; select Test Score as the test variable and click define groups, click continue to close define groups window. Be sure the Test Type selected is Mann-Whitney U, and then click OK.

3. Please clarify the results in detail, what percentage of CG cases had Cox 2 and Bcl2 expression and how can we draw conclusions from studying only 4 cases of ADC that these may be related.
A: Thank you for your suggestion. We have provided the detailed results of percentage of CG cases had Cox-2 and Bcl-2 expression in Table 1. Generally speaking, three cases could be analyzed by statistical method. Even we have only four cases, we performed statistical analysis and results demonstrated the statistically significant difference.