Author’s response to reviews

Title: Early screening the small bowel is key to protect Peutz-Jeghers Syndrome patients from surgery: a novel mutation c.243delG in STK11 gene

Authors:

Zi-Ye ZHAO (yemenzhao@126.com)
Yu-Liang JIANG (sting_321@163.com)
Bai-Rong LI (airbai8040@163.com)
Jing LI (lijing@yeah.net)
Xiao-Wei JIN (jinxiaowei@yeah.net)
En-Da YU (endayu@yeah.net)
Shou-Bin NING (ningshoubin@126.com)

Version: 1 Date: 30 May 2018

Author’s response to reviews:

Dear Editor,

Thank you very much for reviewing our manuscript entitled “Early screening the small bowel is key to protect Peutz-Jeghers Syndrome patients from surgery: report of a novel STK11 mutation (c.243delG)” (ID: BMGE-D-17-00567) very carefully and giving us an opportunity to revise it. We appreciate the editor and reviewers very much for their constructive comments and suggestions on the manuscript.

We have studied comments carefully, and we have made a careful revision point-to-point. All revised portions are marked with a yellow background in the resubmitted manuscript which we would like to submit for your kind consideration.

Kind regards.

Zi-Ye ZHAO, Yu-Liang JIANG, Bai-Rong LI, Jing LI, Xiao-Wei JIN, En-Da YU and Shou-Bin NING

May 30th, 2017
Corresponding authors: Shou-Bin NING, En-Da YU
E-mail: ningshoubin@126.com
E-mail: endayu@yeah.net

ID: BMGE-D-17-00567

Title: Early screening the small bowel is key to protect Peutz-Jeghers Syndrome patients from surgery: report of a novel STK11 mutation (c.243delG)

Replies to the reviewers’ comments:

Andrzej Plawski, Ph.D. (Reviewer 1):

Comment 1: The PJS is a syndrome increasing cancer risk in various organs. As we know in young boy there is the increased risk of testicular tumors and it may occur at age of 5, but the authors did not mention about any other examination of the patient. It should be added.

Response: We appreciate the reviewer’s comments, and we have added the context of physical examination (page 4 lines 18 and 19).

Shirley V. Hodgson (Reviewer 2):

Comment 1: The English is very poor throughout and requires extensive revision. Some examples include: "got abdomen cramps", "but not in his parents, which is not recorded in databases.", "diagnosis of PJS was affirmed", "endoscopy was applied", "A survey of STK11 gene", "large deletion and missense 17 mutation", etc.

Response: We have carefully checked our manuscript in the language, and the whole manuscript has been reviewed and comprehensively modified by our friend who is a native English speaker. Corrections have been made in the corresponding areas (page 2 line 9, 14 and 15; page 4, line 13, 15 and 28-34; page 5 line 1, etc.).

Comment 2: The mutation is reasonably described, but 50 unrelated controls is an extremely small number to test to see whether it occurs in the general population.
Response: We not only checked it in our controls, but also in the databases like ExAC which includes thousands of people. So we concluded this is a novel mutation (page 5 lines 1-4).

Comment 3: The structure prediction seems good although the picture of the resultant protein is much smaller then the wild type protein. In the figures and the text there is no mention of the classical arborising histology seen in PJS polyps despite it being apparent in the histology slide shown.

Response: Thanks for the important suggestion! We have added the corresponding expressions in the context (page 3 lines 23-24).

Comment 4: The comment that extensive surveillance would be recommended for children from the age of 4-5y is not sufficiently discussed in the context of the disadvantages of such screening in young children, and the fact that the patient described in this paper was found to have symptomatic polyps from the age of 7y. Also it seems worrying that one patient discussed from a quoted literature survey of 22 paediatric patients on surveillance developed a post-Laparoscopic-DBE pelvic abscess. A more critical review of the pros and cons of such screening in children would be appropriate.

Response: We have discussed this issue again in Discussion section (page 6 lines 34-36, page 7 lines 7-9 and 20-21).

Randall W Burt (Reviewer 3):

Comment 1: The authors should give: 1. The fraction of expected de novo mutations in this disease (often stated to be about 25%).

Response: We have checked several articles containing relative large number of PJS patients, and found it hard to calculate this fraction. So we digged ourselves’ database. We have recorded 126 PJS patients with detected STK11 mutations, and 62 of them did not have family history of PJS. So the actual fraction of de novo mutations based on our data is 49.21% (page 6 lines 5-6).

Comment 2: The authors should give: 2. A clear statement of the generally agreed upon screening and surveillance recommendations for the large and small bowel in Peutz-Jeghers syndrome---a table would be good for this. Several papers are quoted, but a summary recommendation would be very helpful.
Response: Thanks for the suggestion! We have added Table 2 to show it clearly.

Comment 3:
Not as relevant to this paper, but nonetheless very important to the management of Peutz-Jeghers syndrome would be a table summarizing the cancer risks and screening guidelines for GI and non-GI malignancies. This is optional but may be very helpful. At least a reference to this information should be given.

Response: Corresponding changes have been made (page 6 line 34-36).