Author’s response to reviews

Title: Nerve Growth Factor and Tropomyosin Receptor Kinase A are Increased in the Gastric Mucosa of Patients With Functional Dyspepsia

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Title: Nerve Growth Factor and Tropomyosin Receptor Kinase A are Increased in the Gastric Mucosa of Patients with Functional Dyspepsia

Dear Editors and Reviewers:

Thank you very much for your comments and giving us the opportunity to revise. Those comments are all valuable and very helpful to the advance of our paper. We have carefully revised the manuscript based on the comments of the reviewers. A point-by-point response is enclosed. We also corrected the spelling and format mistakes in the original manuscript. The revised sections are marked in red in the paper. We hope you find the revision acceptable.

Best regards,

Sincerely yours,

Fei Dai (daifei35@163.com)
Reviewer’s Comments and Detailed Responses

Reviewer reports: Cristina Giaroni (Reviewer 1): This study describes the expression of NGF and its high affinity receptor, TrkA, in the gastric mucosa of patients affected by functional dyspepsia, and the possible correlation with enhanced NGF-TrkA pathway with some of the symptoms associated with the disease. The study has merit. However some points should be addressed before publication:

Background:

Line 30: EGCs are major cellular components of myenteric and submucosal ganglia within the ENS. This information is missing;

Response:

Thank you so much for your careful review of our manuscript. We have added this information to the revision.

Methods:

-Line 5: a second biopsy was used to perform immunocytochemistry…. 
-Line 7: Another

Response:

Thank you very much for your comment. We have corrected the above mistakes in the revised version.

-For immunohistochemistry, immunofluorescence and western blotting procedures there are no indications on the controls specificity assays;

Response:

For immunohistochemistry, immunofluorescence and western blotting procedures, PBS was used as a blank control. We have added this information in revised version.
-Which program was used to measure the NGF, GFAP and TrkA staining density?

Response:

IPP 6.0 software (Media Cybernetics, Maryland, USA) was used to measure the NGF, GFAP and TrkA staining density. We have addressed this information in the revised manuscript.

-There are no specifications on the method used to express western blotting;

Response:

We had expressed the method of western blotting in Page 6 Line 17-36.

-Since, in the mucosa of FD patients, NGF and TrkA may be expressed by different populations of inflammatory cells double staining with appropriate markers (i.e. eosinophils and mast cell) should be performed, to better characterize the possible mucosal sources for the neurotrophin;

Response:

The present study indicated that NGF and TrkA were expressed in the cytoplasm of the gastric epithelial cells, the glandular epithelial cells and the mesenchymal cells of lamina propria including mast cells, eosinophila and EGCs. We placed emphasis on NGF/TrkA signaling in EGCs, so we detected TrkA expression on EGCs using GFAP and TrkA double staining method. However, if the expression of NGF and TrkA on different populations of inflammatory cells were observed using double staining with appropriate markers, the possible mucosal sources for the neurotrophin will be better characterized. We are very sorry for this deficiency and we prepare to study further this in future study

Statistical analysis: please specify the relevant data sets for each applied statistical test

Response:

Following reviewer suggestion, we had specified the relevant data sets for each applied statistical test in the revised manuscript.

Results:

-data indicating the severity of symptom scores to the patients are missing;
Response:

Please find this data in Figure3.

-Lines 13, 29: (Figure 1B). (Line 13) NGF staining density and (line 28) TrkA staining density: would better describe the immunohistochemistry approach;

Response:

According to reviewer suggestion, we have described the immunohistochemistry and immunofluorescence approach in revised version.

Discussion:

-There is no discussion on how the upregulation of NGF-TrkA pathway in the FD patient mucosa may affect afferent sensory neurons for the stomach modulating visceral hypersensitivity;

Response:

We very appreciate these comments about this discussion. We have added relevant content in the revision.

Minor: the English form should be revised by a Mother Language speaking colleague

Response:

Following reviewer suggestion, this manuscript was revised by Nature Research Editing Service (http://bit.ly/NRES_BS).

Abstract

Line 8: .. and motility disorders…;

Line 15: .. in gastric mucosa of patients with FD;

Line 21: remove square brackets after PDS;

Line 23: The expression of NGF, TrkA and GFAP was examined;
Line 40: Changes in the expression of NGF, TrkA and GFAP positively..

Response:

Thank you very much for your careful review. We have corrected these mistakes and added relevant information in revised manuscript.