Author's response to reviews

Title: Implication of Intracellular Localization of Transcriptional Repressor PLZF in Thyroid Neoplasms

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Author's response to reviews:

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Editor-in-Chief
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Dear Editor and Reviewers.

Thank you for reviewing our manuscript entitled “Implication of Intracellular Localization of Transcriptional Repressor PLZF in Thyroid Neoplasms”. We revised this manuscript in accordance with your thoughtful suggestion and comments. As you recommended, we requested native speakers of English in Edanz to proofread and revised our English writing.

We would be very grateful if you consider our manuscript for publication in BMC Endocrine Disorders.

Response to Referee 1

We changed following the term ‘tissue’ incorrectly used.

P3L31: changed from “various thyroid tissue” to “different types of benign and malignant thyroid lesions as well as in normal thyroid tissue”.
P3L37: changed from “all types of thyroid tissues” to “all samples of thyroid lesions” instead “all types of thyroid tissues”.
P3L42: changed from “other tissue” to “thyroid lesions”.
P6L68: changed from “various thyroid tissue” to “different types of benign and malignant thyroid lesions”.
We performed immunohistochemical (IHC) staining in all samples whereas western blot analyses was carried out using four samples of N (cases 1-4), five samples of AL (cases 5-9), and 13 samples of PTC (cases 12-24). We performed immunohistochemical (IHC) staining using four samples of N, five samples of AL, two samples of FA, 20 samples of PTC, and three samples of ATC. The characteristics of analysed samples are listed in Table 1.

The proportions of positively stained cells and the intensity scores were evaluated by two experienced professionals.

We did not discuss enough about translocation of PLZF, so we cited your proposal article. We inserted this article P12L183-186 in revision manuscript.

Legend of Table1: We titled ‘Summary of thyroid neoplasm histotypes studied and patients sex and age distributions’. We added a table footnote to explain CI and LN abbreviations.

Table1: We deleted the line papillary carcinoma, and added PTC before CI, LN.
Response to Referee2

We were not able to discuss it enough about translocation of PLZF as you said. Binding HB-EGF-C was considered as a trigger of export PLZF from nucleus, and it caused decrease of repression of PLZF and progression cell cycle. HB-EGF acts not only exporter of PLZF, but also could be agonist for EGF by itself. Cleavage of HB-EGF becomes the point of various carcinogenesis. As regards thyroid gland, increased expression of HB-EGF was observed in PTC and ATC (Ota et al. oncology reports, 30, 1593-1600. 2013). As you suggested, we strongly suspected that the mechanism of HB-EGF related with thyroid carcinogenesis as well as other cancers when we considered based on these previous papers. We believe we should have included HB-EGF-C and other mechanism for our discussion. We cited articles you proposed and reformulated discussion.

We should analyze the actual role of PLZF and HB-EGF-C in thyroid cell lines and further human thyroid samples. However we do not have enough time to complete the experiments until 17th, June. At this time, we would like to submit only our observations about translocation of PLZF. However, in time to come, we would like to reveal the actual role of HB-EGF-C and PLZF in thyroid using thyroid cell lines and human samples. Now, the number of our thyroid samples is gradually increasing and more of their prognosis are being revealed, therefore we will research a relation between expression of PLZF, HB-EGF and progression of malignancy.

Sincerely,

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