Reviewer’s report

Title: The precursor for nerve growth factor (proNGF) is not a serum or biopsy-rinse biomarker for thyroid cancer diagnosis

Version: 0 Date: 23 Jul 2019

Reviewer: Martin Read

Reviewer's report:

In this study the authors have examined the value of proNGF as a serum and biopsy-rinse biomarker for thyroid cancer diagnosis. Overall, the manuscript is well-written, clear and of scientific importance to inform the wider research community of the value of utilising proNGF as a clinical biomarker in thyroid disease. However, the authors need to address the following comments:

(i) The title reflects the main finding of the manuscript, i.e. that proNGF is not a clinical biomarker for thyroid cancer. However, the authors do show some positive results- i.e. serum proNGF may be a biomarker for hyperthyroidism and for follicular lesions in general. The impact of the manuscript would be greater if the authors introduced some element of their positive findings into the title.

(ii) In Fig 2A it is not clear why there are error bars on the graph. The data appears to be finite percentage values derived from Table 2- i.e. 9/28 hyperthyroid cases (32%) v 19/176 euthyroid cases (11%). Please clarify.

(iii) The authors need to include a new figure (similar in design to Fig. 2B or 2C) comparing serum proNGF values stratified according to euthyroid versus hyperthyroid status. This new figure would be useful to reinforce the findings of Figure 2A/Table 2 showing that proNGF levels are higher in sera from patients who were hyperthyroid at the time of sampling.

(iv) Serum proNGF data provided in Table 2 is a bit unclear as the median serum proNGF values (middle column) for hyperthyroid versus euthyroid status are both shown as zero but a p value of 0.002 is given. In fact the median serum proNGF values for all the different categories (i.e. malignancy, age, sex etc) are set to zero. Please state whether the middle column of data refers to the median value for serum proNGF and the value in brackets are the IQR. The authors should check the median proNGF values in Table 3 as well, which are all set to zero except for the follicular lesions (present) category. Further clarification is required.

(v) The authors need to provide an additional table with individual patient characteristics (n=73) for cases with detectable proNGF from the biopsy rinse procedure (i.e. similar in design to additional table 2 for patients with detectable serum proNGF).
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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No

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