Author’s response to reviews

**Title:** Core I gene is overexpressed in Hurthle and non-Hurthle cell microfollicular adenomas and follicular carcinomas of the thyroid.

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PDF covering letter
Dear Doctor Puebla

Enclosed please find, in attachment, the revised form of the manuscript “CORE I GENE IS OVEREXPRESSED IN HÜRTHLE AND NON-HÜRTHLE CELL MICROFOLLICULAR ADENOMAS AND FOLLICULAR CARCINOMAS OF THE THYROID” that we would like to re-submit for publication in BMC Cancer (Re: MS: 9787278402584186).

The study has been reinforced by a substantial increase in the size of the series (31 cases instead of 16) and the manuscript has been extensively modified following the reviewers’ comments and suggestions. We think we have properly addressed the two major criticisms of the three reviewers: small size of the series and inappropriate quoting of the molecular findings in adenomas and follicular carcinomas. The larger size of the series increased the consistency of the results and allowed more solid conclusions.

The following points were specifically addressed:

**Reviewer #1 (Dr Valeriano V. Leite)**

**Discretionary Revisions**

Point #1. We have added 15 new cases to the original series of 16 cases. The histotypes of the 15 new cases are the following: Follicular carcinoma composed of Hürthle cells (n=5); Microfollicular adenoma (n=4); Papillary carcinoma (n=1); Papillary carcinoma composed of Hürthle cells (n=3); and Macrofollicular adenoma (n=2).

Point #2 We agree with the reviewer’s comment and we have therefore deleted from the Materials Sections the sentence on the absence of L-tyroxine treatment before surgery.

Point #3. This point was addressed according to the reviewer’s suggestion. In Table 2 (page 23) the sentence *Genes overexpressed in the corresponding normal thyroid tissue: was substituted by Genes underexpressed in the tumour:*

**Minor Essential Revisions**

Point #1. **Background (page 3 - paragraphs 2 and 3) -** We fully agree with the reviewer’s criticism and the text was re-written accordingly (PAX8 – PPARgama fusion gene is indeed associated with follicular carcinoma and not with hyperfunctioning adenoma). We have also improved the review of the literature and included more detailed data on molecular alterations of thyroid neoplasms.

Point #2. **Material and Methods - Differential display (page 5) –** There was a mistake in the text (2nd paragraph, line 15): instead of Table 2 it should be written Table 1. The sequence of D390 primer is now represented in Table 1.
**Reviewer #2 (Dr Sylvia L. Asa)**

*Minor Essential Revisions*

We have rewritten the Introduction taking into consideration the reviewer’s criticisms. We fully agree with the specific point raised by the reviewer (As a matter of fact we can not explain how the text was miswritten). The mistake was corrected (see answer to reviewer #1) and we have also improved the review of the literature and included more detailed data on molecular alterations of thyroid neoplasms.

**Reviewer #3 (Dr Todd G. Kroll)**

*Compulsary issues*

We have addressed one of the two criticisms of this reviewer: the small size of the original series. In order to improve the study, we have added 15 new cases, including: 5 Follicular carcinomas composed of Hürthle cells; 4 Microfollicular adenomas; 1 Papillary carcinoma; 3 Papillary carcinomas composed of Hürthle cells and 2 Macrofollicular adenomas. The results obtained in the analysis of the new cases supported our previous conclusions.

With regard to the second point we agree with the reviewer’s comment that the use of other techniques would improve and strengthen the study. Unfortunately, however, it does not seem possible to perform western blotting or immunohistochemistry, since, to our knowledge, there is no anti-Core I antibody available. Regarding the possibility of performing northern blots, which we think is also a very good suggestion, the scarcity of available material does not allow the extraction of sufficient amounts of RNA.

Looking forward to hearing from you, I remain

Yours sincerely

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