Reviewer's report

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

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Reviewer: Valeriano V Leite

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Máximo et al. applied the method of differential display to search for genes involved in the pathogenesis of follicular thyroid carcinomas composed of Hürthle cells. The differential display analysis of a case of follicular Hürthle cell carcinoma revealed three genes that were upregulated and four genes that were downregulated compared to the corresponding normal thyroid tissue. One of the overexpressed genes was particularly interesting because it was identified as the Core I subunit of the complex ubiquinol-cytochrome c-reductase (complex III) of the mitochondrial respiratory chain. The levels of expression of this gene were then analysed by semiquantitative RT-PCR in sixteen thyroid tumours with or without Hürthle cell features. Core I gene overexpression was detected in 4/4 follicular carcinomas, 1/1 medullary carcinoma, 4/7 follicular adenomas, and 0/5 papillary carcinomas, normal expression in 3/5 papillary carcinomas, and underexpression in the remaining cases (3 follicular adenomas and 2 papillary carcinomas). There was no correlation of Core I overexpression with malignancy, Hürthle cells, or proliferative (MIB-1) activity of the tumour. However, a significant correlation was found between Core I overexpression and the microfollicular pattern of growth of thyroid tumours.

General comment:

This is a very well-written and technically sound paper. The original contribution of this manuscript relates to the correlation that was established between Core I overexpression and the microfollicular pattern of growth of thyroid tumours. However, the number of samples tested was relatively small, as acknowledged by the authors on page 15 (Conclusions).

Discretionary Revisions

1-The manuscript could be improved by analysing more samples of tumours with a microfollicular pattern of growth.
2-Materials (page 4). I do not understand the relevance of saying that the patients were not treated with L-thyroxine before surgery.
3-Table 2 (page 23). It seems more appropriate to subdivide the differentially expressed genes in genes overexpressed and underexpressed in the tumour.

Minor Essential Revisions

1-Background (page 3). I do not agree that PAX8/PPARgamma fusion gene is more consistently associated with (functioning?) thyroid adenomas than with thyroid follicular carcinomas. Most of the published data show that this rearrangement is more prevalent in follicular carcinomas than in adenomas. For instance, in the reference provided by the authors (ref. 5) the fusion gene was detected in carcinomas, but not in adenomas.
2-Differential display (page 5). The nucleotide sequences of primers D433, D492, and D495 are shown in Table 1 and not in Table 2, as indicated by the authors. The nucleotide sequence of D390 is not represented in the Table.

Major Compulsory Revisions

None.

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

None.