Reviewer’s report

Title: NKX2.5 is expressed in papillary thyroid carcinomas and regulates differentiation in thyroid cells

Version: 0 Date: 03 Oct 2017

Reviewer: Kevin Fisher

Reviewer’s report:

In this study by Cardoso Penha and colleagues, the authors evaluated NKX2.5 expression in a validation and exploratory cohort of thyroid carcinomas. They performed a clinicopathologic analysis with the IHC results and concluded that NKX2.5 expression was associated with a better prognosis. Also, in vitro assays demonstrated that NKX2.5 overexpression reduced the expression of thyroid differentiation markers and increased ROS production suggesting a possible role for NKX2.5 overexpression in thyroid carcinogenesis.

Major Comments:

1. The in vitro experiments were well conceived with appropriate controls and design. I have no major comments regarding the in vitro assays.

2. Table 2 refers to a bivariate analysis, but the way the data are displayed it is misleading as to indicate a non-bivariate analysis. It would be helpful to the reader to make it clear that the NKX5.2 expression (low and high) were grouped together for statistical analysis.

3. Also, were the authors able to discern whether cytoplasmic/nuclear or low/high staining afforded any prognostic impact? I acknowledge that the N is low but this may be important given the variable staining pattern, and the authors' hypothesis that cytoplasmic sumoylation may account for the aberrant localization.

Minor Comments:

1. Please use HGNC nomenclature throughout. When referring to the protein, the protein name (e.g NKX2.5) should be capitalized and non-italicized. If referring to the gene that encodes the protein, the gene name is capitalized and italicized (e.g. NKX2-5).

2. The methods state that you studied both 51 and 53 patients. Please correct.

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?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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