Reviewer's report

Title: Large intragenic deletion of CDC73 (exons 4-10) in a three-generation hyperparathyroidism jaw tumor (HPT-JT) syndrome family

Version: 0 Date: 26 Jan 2017

Reviewer: William F. Simonds

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In this manuscript, Guarnieri et al conduct germline CDC73/HRPT2 mutation analysis in a family with hyperparathyroidism-jaw tumor syndrome (HPT-JT) in which the proband was found to have parathyroid cancer. The authors confirm carrier status of the proband's daughter, and uncover a positive history of HPT in the proband's father. A novel deletion of exons 4 to 10 of the CDC73/HRPT2 gene was detected in the three affected family members. In addition, a novel single-base insertion in the 5'UTR that co-segregated with the large intragenic deletion was identified. The 5'UTR single-base insertion was shown to significantly impair the expression of the parafibromin protein in in vitro assays.

This work emphasizes the importance of screening for large deletions in CDC73/HRPT2 in kindreds with possible HPT-JT or even familial isolated HPT, even when initial PCR-based screening for CDC73/HRPT2 germline mutation is negative, when there is a high index of clinical suspicion.

Minor suggestions:

a) In the abstract (p. 3 line 12) "co-segregated" is misspelled.

b) Please add a reference (e.g. on page 6, line 3), for the benefit of the less specialized reader, regarding the association of uterine neoplasia and dysplasia with HPT-JT and CDC73/HRPT2 mutation.
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?
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Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

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I am able to assess the statistics

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