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: 10 Mar 2017

Reviewer: Jessica Mester

Reviewer's report:

This article was nicely written and contained valuable information about an interesting and rare disorder. I would ask the authors to address a few points below, and I look forward to seeing this article in publication.

1. Based on the co-segregation of the 5' UTR variant and large deletion, these variants are occurring on the same allele (in cis) in this family. Given that the large deletion is likely to result in nonsense-mediated decay (NMD), do the authors believe the 5' UTR variant would ultimately have any impact in this situation? If the answer is "no" given the predicted NMD it would be beneficial to the reader for the authors to state as such. I do appreciate that the authors did not ascribe any clinical significance to the presence of this variant or try to suggest that its presence modified phenotype in any way.

2. I appreciate the authors' noting the presence of polymorphic variants within the 5' UTR region discussed. I'd also direct the authors to review the variants identified in this region in the ExAC (http://exac.broadinstitute.org/) and gnomAD (http://gnomad.broadinstitute.org/) browsers, which include population data with much higher allele counts than the resources noted on page 10, lines 5-7, and consider incorporating that population data into their discussion.

3. In looking at the conservation of the region where the insertion occurs, I found myself disagreeing with the authors' assertion that the region was "absolutely conserved from humans to rodents" (page 10 line 8). Per the UCSC genome browser, which calculates conservation using PhyloP, conservation appeared poor at a few nucleotide positions in the region of interest, appearing very poor at c.-5 even among apes and rodents. I'd ask the authors to soften their language with respect to the conservation of this region.
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

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?
If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I work for a clinical laboratory that offers deletion/duplication testing for the gene described in this article, a methodology not offered by all clinical laboratories. The article discusses that this methodology is valuable and should be pursued in patients with clinical suspicion for a CDC73 mutation. Persons reading this article may opt to send their samples to one of the laboratories, including ours, that offers this service.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal