Reviewer’s report

Title: Familial inheritance of the 3q29 microdeletion syndrome: case report and review

Version: 1 Date: 18 Dec 2018

Reviewer: Jill Anne Rosenfeld

Reviewer’s report:

Most of my previous concerns have been addressed. A few remain that could benefit from additional clarification:

1. Review of previously reported smaller deletions: The citations in the discussion appear to cite the paper with the first author of Coe instead of Cox. Additionally, the previously mentioned paper (Mulle et al. 2014, PMID 23871472 describes the characterization of a de novo smaller 3q29 deletion in the supplement; this is the same case from Mulle et al. 2010 PMID 20691406. Additionally, the authors could consider including a statement about conclusions that could be made from the smaller deletions in the paragraph in the discussion. For example, do these smaller deletions provide support for the role of the candidate genes in this syndrome?

2. Possibility of underascertainment: This is a relevant concern, when it comes to identifying deletion carriers through clinical testing, as some individuals will likely not raise sufficient suspicion to lead to clinical genetic testing. However, it might be misleading to only tie the underascertainment to a population-based incidence. True, ethnicity stratification has not been accounted for, but there is no evidence whether this would lead to under- or over-estimation of incidence. The background may, therefore, benefit from further separation of estimation of incidence from the problem of underascertainment.

Additional points:

1. Background, first sentence: the addition of the clause about detection of relevant CNVs from sequencing studies could be rephrased, as the beginning of the sentence is focused on the use of CMA.

2. Discussion, last paragraph, second sentence: "given" is misspelled.

3. Figure 2 legend:
   a. Green & blue dots are mentioned - should be red & blue?
   b. 3rd sentence: the authors could consider rephrasing, as the mention of the dotted lines makes one think it may be referring to the bottom panel, but then it mentions
the values on the y-axis, which references the top panel. Additionally, the "2" in log base 2 should be in subscript.

c. 4th sentence: "user-defined" is missing the final 'd'.

d. Panel D description: the same FISH probe name is mentioned for both probes.

4. Table 1, footnotes: the mention of a transmitting grandmother as "patient 11" may benefit from clarification - the mother represents the 11th case of parental transmission.

**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.

Not relevant to this manuscript

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