Author’s response to reviews

Title: Genotype-phenotype correlation in 22q11.2 deletion syndrome

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Version: 2 Date: 29 November 2012

Author's response to reviews: see over
November 27, 2012

Dear Dr. Slavotinek,

Thank you very much for your attention and positive response to our paper (MS: 1945955094759096). We appreciate the careful reading that you and the reviewers have given the paper, and the invitation to revise and resubmit it. We feel that the paper has been improved by this process, and hope that it is now acceptable for publication in *BMC Medical Genetics*.

Below, please see our point-by-point response to the comments of the two reviewers. The comments are in regular font and our responses are in bold.

Referee 1 (AS):

1. “Mean age 16.1±9.7;” - you should state months or years.
   - We added the correct unit "years" (Section: METHODS, Subjects)

2. “We elaborate below on the clinical features of this patient because it carried a rare deletion with only two other similar cases in the literature” –she rather than it
   - We changed “it” to "she" (Section: RESULTS, Case report)

3. “T. was referred to our clinic” – patient initials should not be used.
   - All "T."s were changed to "She" or "Patient VC901" (Section: RESULTS, Case report)

4. “Already in preschool she was diagnosed with…” – please state age.
   - was changed to "Already at the age of 5 years she was diagnosed with.." (Section: RESULTS, Case report)

5. “VSD” – please spell out; same for “VIQ”
   - "VSD" and "VIQ" were spelled out: "ventricular septal defect" (Section: RESULTS, Case report), "Verbal IQ" (Section: DISCUSSION, penultimate paragraph)
6. “Thus the MLPA is clearly superior to FISH as a diagnostic tool and a useful method for deletion characterization, essential for genotype/phenotype analysis.”
   – you should mention that array is another technique that would have detected an atypical deletion although costs of performing it may be higher.
   - A sentence stating "CGH and SNP array techniques can also detect atypical deletions but their costs are substantially higher." was added. (Section: DISCUSSION, first paragraph)

7. “…and the high throughput methods of the near future e.g..” –can remove near future, as the methods are already used.
   - This part of the sentence was changed to ".....and the high throughput methods such as ...." (Section: CONCLUSIONS, first paragraph)

Referee 2 (BL)
1. Consider taking out your analysis of PRODH as it does not seem to add to the paper.
   - PRODH is an important candidate gene for the neuropsychiatric pathology in 22q11.2DS and in the general population (Refs. 22, 23) and thus we think that it should be included in the manuscript.

2. Figure 3: Please consider adding the clinical findings in the text (i.e. Facial appearance of patient including broad square face, hypotelorism, etc.....).
   - The clinical findings were added to the legend of Figure 3.

In addition, an Acknowledgement section was added between Authors' contributions and References, acknowledging the funding of the study.

Sincerely,

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