Author's response to reviews

Title: Discontinuous microduplications at chromosome 10q24.3 identified in a Chinese family with split hand and foot malformation

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Author's response to reviews: see over
Dear Editor,

Thank you for considering our manuscript for publication pending revisions. The following is the response to reviewers' comments.

Reviewer: Fiorella Gurrieri

(1) I agree with the hypothesis that the identified duplications contain regulatory sequences that may upregulate or down regulate limb developmental genes. However I think it is important to add expression data on the genes included or disrupted by the duplications. I suggest to perform real-time on cDNAs of these genes.

We appreciate the valuable comment and agree that the expression data of the genes would add valuable information. However, the stored blood samples were unable to extract total mRNA to perform real-time on cDNAs of these genes.

(2) I suggest the Authors include a scheme of the double duplication including the different sizes observed.

Done as suggested. We added a scheme of duplications as supplementary materials.

(3) The Authors should check on the DPCD nomenclature.

DPCD is short for deleted in primary ciliary dyskinesia homolog (mouse). The gene ID in NCBI database is 25911. We have added the information and other abbreviations to the manuscript.

Reviewer: Giovanni Neri

(1) The authors report on an interesting genomic rearrangement in a family segregating SHSF malformation. They state that all family members were carefully evaluated clinically. Did that evaluation include X rays?

Yes, all family members were examined by X-ray. But we only have the hard copies of three patients.

(2) However, molecular analysis seems to have been conducted only on three (unspecified) unaffected individuals. If that is the case, I recommend that the molecular analysis be
extended to all family members, given that a defect of penetrance is well known in SHSF.

Genome-wide copy number variation analysis was performed for four affected and two unaffected individuals. But candidate gene mutation screening and real time qPCR were conducted for all available family members (4 affected+14 unaffected). We have clarified it.

(3) In the clinical report, the authors state that there are six affected individuals in the family, but in the pedigree I see only five.

There are five affected individuals in the family. We corrected this error in the manuscript.

(4) On p. 7 the authors refer to the posterior part of the FBXW4 gene. What does posterior mean?

It indicates the 3′ end of the gene. We rewrote this sentence.

(5) The MS is generally well written, but the English can benefit from some improvement.

Done as suggested.

Once again, thank you very much for your constructive comments. Please let me know if you have any additional comments.

Sincerely,

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