Author’s response to reviews

Title: Case report: two novel VPS13B mutations in a Chinese family with Cohen syndrome and hyperlinear palms

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Editor Comments:

Q1: parental permission for publishing children's photo should be declared.
ANS1: According to Editor’s suggestion, we have re-checked the permission files, and declared that ‘Parental permission for publishing patients' photo was obtained’ in the methods section.

Reviewer1:

Q1: The VPS13B p.K3282X mutation is a nonsense mutation, not a missense mutation. Nonsense mutations insert a premature stop codon within the reading frame while missense mutations simply can the amino acid sequence.
ANS1: According to Reviewer’s suggestion, I have changed the missense mutation to nonsense mutation throughout the manuscript.

Q2: The rationale for using exome sequencing for this family instead of more direct targeting sequencing of the VPS13B gene is not provided. Since most, if not all, Cohen syndrome cases are associated with mutations in VPS13B, would it not make better sense to sequence this gene first instead of using the more expensive, more labor intensive and more data intensive exome sequencing approach?
ANS2: Truly, Cohen syndrome cases are associated with mutations in VPS13B. However, due to VPS13B mutated CS cases was rarely reported in Chinese, CS is a clinically heterogeneous disorder, and some phenotypes of CS are unobservable before 10 years old, we cannot consider the VPS13B gene. On the other hand, in clinic, mentally retarded and underdeveloped patients are often seen with
very complicated reasons. Therefore, we first carried out the GTG-banding, then the CNV array, and then carried out the exome sequencing, for the family.

Q3: Figures 1 and 2 should be merged into a single figure.
ANS3: According to Reviewer’s suggestion, I have merged the Fig 1 and Fig 2 to a single one.

Q4: The authors state, on more than one occasion, that "China is the most populated country in the world." What is the relevance of this statement to this manuscript?
ANS4: Our original intention is that China is the most-populated country, but only few CS patients have been reported. Nevertheless, in order to avoid "misunderstanding" as much as possible, we have deleted two places where ‘China is the most populated country in the world’ appeared throughout the manuscript.

Q5: The quality of the written English in this manuscript is poor. The authors should consider soliciting editorial assistance.
ANS5: This paper was revised by international paper editing service (Enpaper.com). The revising work was performed by a subject expert editor and approved by two senior editors. All our editors are native English speakers.

Reviewer2:

Q1: Venkateshwari Ananthapur, Ph.D (Reviewer 2): The manuscript was well presented. Please provide update of the case reports in other populations.
ANS1: According to Reviewer’s suggestions, we have added the following description to the introduction of the revised manuscript: Recently, several VPS13B mutations have been reported in CS families which from Tunisia and Pakistan [6-7].