Author's response to reviews

Title: A Novel Single Base Pair Duplication in WDR62 Causes Primary Microcephaly

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Cover Letter

Dear Editor,

We are pleased to add the following revisions as per reviewers’ instructions:

Referee 1:
1. We changed confirmation to conformation at Lanes 30 and 147
2. Deleted sentence “It also opens many insights into disease understanding.” At Lanes 32-33
3. Deleted “(Roberts et al. 1999)” at Lanes 51-52
4. In table 1, reported mutation by McDonell et al 2014 have been inserted.
5. Figure 1 and 3 are combined and a single Figure 1 has been generated
6. Figure 2 and 4 are combined and a single Figure 2 has been generated

Referee 2:
1. We used the bioinformatics to predict the effect of single base pair duplication and Figure 5 is illustrating the effect of mutation. Part a presenting the secondary structure features of the gene and difference of these structure elements in both normal and mutated forms of the gene which is important and according to the current study. Part b is showing conservation of amino acid that how much it is important in the sequence. Secondly hypothesis is a major step of scientific method. By this study we not only showing conservation of amino acid and sequence but also hypothesizing that the mutation can also affect these species likewise Human.
2. This is not SNP and we need to read the sequence from start to understand it fully. As we have shown the sequencing chromatogram in Figure 4 to highlight the duplications in WDR62.

3. Microarray and sequencing resulted clearly shown the mutation and also confirmed that there is no mixing of DNA. We cannot assume anything after confirmation of results on samples.

4. The following paragraph is added as reviewers recommendation in lane #21. MCP1-2 (Fig. 1A) had a head circumference of only 37.47cm and a height of 91.44cm. He was reported to show aggressive behavior, being unable to walk due to a disabled left leg and to have an abnormally watery mouth. Beside a head circumference of only 35.94cm and a height of 74.93cm his 2 year old brother, patient MCP1-5 (Fig.1B), displays no other abnormalities.

The third 25 years old patient, MCP1-6 (Fig.1C), has a head circumference of 39.37cm and a height of 170 cm. As for patient MCP1-2, aggressiveness and a watery mouth have been observed. The computerized tomography (CT) scan of this individual revealed reduced volume of right cerebral hemisphere and prominent extra axial cerebrospinal (CSF) spaces with ill defined gryal and nuclei pattern (Data not shown here). However, no local area of brain attenuation and intracerebral blood was observed. Due to the non-cooperative behavior of two other affected individuals (MCP1-2 and MCP1-5) detailed magnetic resonance imaging (MRI) scan could not be performed.

5. Conclusion is self-explanatory indicating the novel mutation is the family.

6. Ethical approval was provided earlier with the submission and informed consent were presented to the ethical committee for approval of study.