Reviewer's report

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

Version: 3 Date: 25 June 2014

Reviewer: Muhammad Hassan

Reviewer's report:

Dear Editor

Thank you for selecting my name as a reviewer for this manuscript. The suggestions below will make this manuscript more comprehensive.

Major Essential Revisions

1- In abstract and elsewhere, authors mentioned about structural changes in the protein WDR62 with this insertion of G in the coding region (although authors mentioned it as duplication everywhere which is inappropriate). They use bioinformatics to predict the pathology of the insertion by portraying conservation of aspartic acid among different related species. But they have to focus on effects of NMD in this case as premature stop is there 3 AA after insertion, hence, most probably there would be no full length mRNA. Therefore, to me there is no space for figure 5 at all. Related debate in computational analysis is secondary and should have less space in manuscript.

2- In figure 4, the sequencing chromatogram, the very first nucleotide should be T and not A, as it is mentioned in reference sequences in ENSEMBL and UCSC (TGCTAGGGGinsGACG). Is it an SNP?

3- For normal individual MCP1-3, the explanation about presence of homozygous marker allele pattern and heterozygous insertion of “G” may not be appropriate. As LOD score is not calculated, one can even delete that individual from genotyping. There might be some mixing of DNA samples etc.

4- Patient presentation is poor in Findings section. HC should be given with SD from the mean. We have no MRI or CT images for any of the patients, therefore any comments about effect of mutation in terms of phenotypic variation is not possible. Authors should try to get brain scan images if possible. Also patient MCP1-2 was unable to walk due to problem in left leg. Is there any X-ray available? Was it a polio affected Leg or congenital. Authors should focus on it as it is never reported previously with WDR62 mutations or even in other MCPH cases. As SD is not given for height (should be given for comparison), I cannot predict presence of seckel syndrome in this family.

5- In conclusion, authors fail to conclude from their own results. Better to write something about your own mutation and its effects. Also there is no need to mention about consent under this section.

6- As per files provided to me, a letter on the behalf of departmental ethical
committee is attached about approval of the project. Authors mentioned (at the end of conclusion) that written informed consents are also attached, but not reached me. In methods section authors should write about approval from departmental ethical committee.

I need to see this manuscript again after incorporation of suggestive changes.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests