Reviewer’s report

**Title:** The effect of homozygous deletion of the BBOX1 gene on carnitine level and fatty acid beta-oxidation

**Version:** 2  **Date:** 12 February 2014

**Reviewer:** Ayman W El-Hattab

**Reviewer’s report:**

The authors presented a girl with homozygous 11p14.2 deletion that encompasses BBOX1 gene which encodes the last enzyme of de novo carnitine synthesis. Despite the fact that such deletion has not been previously reported in the homozygous state, there are several major concerns in this report:

1. The literature review is incomplete and this case is not the first reported patient with complete deficiency in de novo carnitine biosynthesis. Deletions of TMLHE gene (on chromosome X) also result in deficiency of de novo carnitine synthesis (Celestino-Soper PB, et al. Proc Natl Acad Sci USA. 2012;109:7974-81).

2. Making inappropriate conclusions. The acylcarnitine profile and carnitine levels are basically normal. Having a free carnitine level that is closer to the lower limit of normal and such slight increase in AC/FC are not clinically or biochemically significant, especially that this test was done once. So, this acylcarnitine profile results cannot be used as an evidence of carnitine biosynthesis defects and should not receive such emphasis in this report.

3. Including irrelevant details in this report. There is no need to present normal values (e.g. tables 2 and 3) and data that do not add significant and relevant information (e.g. pedigree and brain MRI pictures).

4. The failure to include important and relevant points like details about what is currently known about the other gene (FIBIN) and measurements of intermediates of carnitine biosynthetic pathway.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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