Reviewer’s report

Title: Insertion of an extra copy of Xq22.2 into 1p36 results in functional duplication of the PLP1 gene in a girl with classical Pelizaeus-Merzbacher disease

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Reviewer: Toshiyuki Yamamoto

Reviewer’s report:

Functional duplication of PLP1 was confirmed in a female patient with Pelizaeus-Merzbacher disease. The duplicated region was inserted into 1p36 region. In the breakpoint 2-bp microhomology was confirmed. This study is very suggestive for us to understand structural abnormalities of the genome. There are some questions.

[Major]
1. As the authors mentioned in the text, there is a triplicated segment in the duplicated region. This triplicated region seems to be the region of H2BFXP. To clarify this, it is better to describe exact location of the triplicated segment.
2. Existence of the triplicated segment indicates the duplication-inverted triplication-duplication (DUP-TRP/INV-DUP) as a mechanism not FoSTeS. This should be discussed. Generally, in cases of DUP-TRP/INV-DUP, the telomeric region from H2BFXP would not be duplicated.
3. FISH was performed using a BAC clone PR11-832L2 only. It may be interesting to use probes from the more telomeric region, which may not be inserted into 1p36 region. This reviewer is interested in the location of this segment.
4. Are there any copy number aberration in 1p36 region? This should be clarified.

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.

Declaration of competing interests:

I declare that I have no competing interests.