Reviewer's report

Title: A novel Bruton’s tyrosine kinase gene (BTK) missense mutation in a Chinese family with X-linked agammaglobulinemia

Version: 2
Date: 6 July 2014

Reviewer: Melinda Erdos

Reviewer's report:

Authors have described a novel BTK missense mutation in a Chinese family with X-linked agammaglobulinemia. The language of the manuscript is reasonable.

Major Compulsory Revisions:

1. Paragraph “Case Presentation”, line 71: it would be better to give the absolute count of CD19+ B-lymphocytes rather than the percentage

2. Figures 1 and 2 have to be modified into one figure. Electropherograms have to be showed under the family tree, and have to be indicated by the number of the family member (eg: “III.1” for patient, etc; and “C” for control). Symbols used in the family tree (Figure 2) are completely surprising. The authors should take into account the standardized human pedigree nomenclature and symbols. In a case of an X-linked disease, affected males should be indicated with solid squares (instead of a half shaded square), and female carriers should be indicated with a circle that has a dot inside (instead of a half shaded circle). In the II. generation of the family tree husbands are completely unnecessary to indicate and number, so the list in Paragraph “Genetic analysis”, line 87 correctly is the following: (I.1, II.1, II.2, II.4).

3. The literature is not appropriately cited. All but one reference were published before 2005. It would be important to refer newly published papers; especially those which based on cohort studies give comprehensive overview of the molecular genetic and demographic features of XLA.

Questions:

4. What was the method of the genetic analysis of BTK gene?

5. What was the clinical history of the affected other sibling in this family?

6. Are there other disease-causing nucleotide changes in position c.1117 described before?

7. The patient receives IVIG substitution only in every 2-3 months, rather than in every 4-6 weeks, as in XLA patients it used to. What is the reason for that?

8. Did the authors perform any assay to predict the functional consequences of the novel mutation at protein level?

Minor Essential Revisions:

9. In the text Figure 1A is not mentioned.
10. Paragraph “Introduction”, line 43: “that” is repeated
11. Paragraph “Case Presentation”, line 51: “anti-viral” is not needed
13. Paragraph “Case Presentation”, line 59: it is not clear what “(+++)” means after streptococcus pneumonia
15. Paragraph “Case Presentation”, line 69: “immunodeficiency” is not needed
16. Paragraph “Discussion”, line 134: “in” is repeated
17. Paragraph “Abbreviations”, line 165: the abbreviation of allophycocyanin is missing and it is also not found in the text
18. Paragraph “Abbreviations”, line 165: the abbreviation “IVIG” is not for “gammaglobulin replacement therapy”

**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