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: 11 July 2014

Reviewer: Jer-Ming Chang

Reviewer’s report:

Major Compulsory Revisions

In the “Discussion”, authors chiefly described what are mostly already known. However, the discussion related with the analysis itself is lacking. I suggest that authors may consider to discuss the cost-effectiveness of such an analysis, especially if it concerns the future treatment with IVIG. Also, readers would like to realize if IVIG is the only way of treatment and how about the effect of IVIG in other reports? Are there other treatment options? Please discuss some more content about the past publication on this topic.

Minor Essential Revisions

1. The first sentence of the Introduction: “X-lined ……. is the first primary immunodeficiency disease (PID) to be identified”. I wonder why this rare disorder is the first PID to be identified? In which condition? Please explain or rephrase. Or, the “to be” should be omitted?

2. The second paragraph of the Introduction: “one these 5 domains”. Should it be “one of these 5 domains”? Also, according to my recollection, the five domains should be PH, TH, SH3, SH2, and TK, but not SH1. Please verify.

3. In the Case Presentation, authors mentioned the name of Streptococcus pneumonia. As a general rule, the name of the bacteriae should be italicized (oblique).

4. In the last paragraph of Discussion: “The serum IgG levels were also monitored and maintained above 5 g.” Please explain what does it mean to maintain IgG above 5g?

5. What is the clinical status of individual III-2? Is he also an XLA patient? There should be 2 males being affected in this family, thus in page 5, line 140, a total should be 2 males.

6. In page 5, line 134 " in the in exons" should be "in the exons"

7. In Figure 1: Please consider to put DNA chromatograms A, B, and C in a row and adding the amino acids on top of them for better expression.

8. In Table 1: Formal binomial nomenclature should be used, like H. Sapiens for human.

9. The index case is very young. Authors may have to provide the description of
the vaccination records.

Discretionary Revisions
None

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

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I do not have any financial competing interest concerning the topic.

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- Do you have any other financial competing interests?
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- Do you have any non-financial competing interests in relation to this paper?
I am one of the authors in the paper “Atypical X-linked agammaglobulinaemia caused by a novel BTK mutation in a selective immunoglobulin M deficiency patient. BMC Pediatrics 2013 Sep 27;13:150.”