Reviewer's report

Title: The significance of Notch ligand expression in the peripheral blood of children with hand, foot and mouth disease (HFMD)

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Reviewer: Xingliang Shen

Reviewer's report:

General comments

This report documents Notch ligand expression in the peripheral blood of children with Hand, foot and mouth disease (HFMD). The Notch ligand DII4 shows a correlation with CD3+, CD3+CD8+ and CD3-CD19+ cell subsets, indicating a potential association with HFMD. The data are of interest for the pathogenesis of HFMD. A better understanding of the signal-transduction pathways involved in the pathogenesis (proinflammation cytokines, cells, pathways) and immune responses will be expected to be of value in diagnose, treatment of and vaccine development against the HFMD caused by EV71, CVA16 and other enteroviruses. The manuscript should be considered for publication in the Journal if authors made some modifications.

Major Compulsory Revisions

1. Footnotes of Tables 1, 2 and 3.

Please clarify in footnotes (or in Methods) how the authors calculated the means and SD. Are the numbers the geometric means or arithmetic means of individuals in each group? Authors should how many cells were acquired for FACS assays so that the readers could be able to compare the data with those from other publications.

2. Figure legends (or Methods) should be rewritten.

The authors should explain in detail that, for example, each spot represent a case in all figures and the line represents the average level of the expression of each protein in Figures 1 and 2.

3. Also, it is better to clarify if the expression levels of DII1 and DII4, jaggad 1 and jaggad 2 were ratios of normalized mean of GAPDH and how the relative quantification were performed for the genes in each group in legends of Figure 1 and 2 or in Methods section.

4. The authors mentioned the counting of WBC and determination of total protein concentration in Methods and Discussion, but the results were not described in the Results section. The readers may be interested to know what the differences were in these two indicators between the HFMD group and the control group without HFMD, and between the uncomplicated HFMD group and HFMD with encephalitis group.
5. What is the volume used for WBC counts?

Minor Revisions

The latest data in 2012 and 2013 and from 2008 to 2012 on HFMD from Chinese CDC should be cited in Background section (reference 1) (see Chinese CDC website and a reference below in blue). For example, in 2012 the reported cases of HFMD peaked at 2,198,442 causing 250 fatal cases in China.


Discretionary Revisions

The virus identification should be included, if possible, by performing a quantitative real time PCR or conventional RT-PCR using samples from the patients. The readers may be interested in knowing how many cases were caused by EV71 or CVA16 or other enteroviruses (or unidentified viruses). Also, it is interesting to find out if there are any differences in these indicators investigated between cases caused by EV71 and CVA16.

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

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.