Reviewer's report

Title: BAFF promoted proliferation of human mesangial cells through interaction with BAFF-R

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Reviewer: Xiong-Zhong Ruan

Reviewer's report:

Reviewer's report: minor essential revisions

Comments to authors:

This study investigated the effect of BAFF on the expression of BAFF receptors and the involved downstream signaling transduction pathways in human mesangial cells. Results showed that BAFF led to rapid phosphorylation of NF-κBp65, Akt, and MAPKp38 kinase and imposed cell proliferation in human mesangial cells. BAFF-R is evidently expressed on the cell membrane of human mesangial cell. The phosphorylation of Akt was very sensitive to blockade of BAFF/BAFF-R binding. BAFF treatment resulted in decreased expression of BAFF-R, which implied a negative feedback regulation of the BAFF/BAFF-R interaction.

The most important and interesting findings in this manuscript are that human mesangial cells express BAFF-R and that BAFF/BAFF-R interaction promotes mesangial cell proliferation by activating Akt, p65, and p38 signaling. There are several points should be concerned by the authors.

Q1: In Figure 1, the effect of BAFF on mesangial cell proliferation is important. All the cell proliferation experiments in the manuscript were performed at 48h. Perhaps, authors should also do time-courses to optimize the ‘peak time’ for the cell proliferation under action by BAFF. As demonstrated by authors, BAFF decreased BAFF-R expression at 6h (explained as a ‘negative feedback regulation’). Due to the importance of the interaction of BAFF and BAFF-R on the downstream signaling, a short-term experiment for cell proliferation assay should be performed. This will improve the quality of the manuscript significantly.

Q2: In Figure 3, authors demonstrated that human mesangial cells express BAFF-R using real-time PCR. What is the absolute level of BAFF-R in comparison with a well-known mesangial cell marker (positive control?). It is also interesting to know if mesangial cells express BAFF.

As shown in Figure 3C, the BAFF-R positive cells are only 8.4%, suggesting that there may be different subgroups (BAFF-R positive and negative) of mesangial cells which may have different functions. In this case, the potential positive downstream effects including cell proliferation, inflammatory response and fibrosis may be diluted if the experiment were carried in whole cell population. Targeting BAFF-R positive cells by dual staining technology using BAFF-R and
targeted protein markers of cell cycle protein, inflammation and fibrosis will enlarge/change the biological effects as demonstrated in the manuscript.

Q3: What are the long-term (48h) effects of BAFF on the markers shown in Figure 5?

Q4: Full names should be given for all the abbreviations in the text at the first mention in the text.

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

**Declaration of competing interests:**

no competing interests