Reviewer's report

Title: Antagonism of cannabinoid receptor 2 pathway suppresses IL-6-induced immunoglobulin IgM secretion

Version: 1 Date: 1 November 2013

Reviewer: Santhi Gorantla

Reviewer's report:

Xie et al showed that cannabinoid 2 receptor (CB2R) antagonist or inverse agonist blocks the IgM secretion in SKW 6.4 B cell line induced by IL-6, and this blockade can be stopped by CB2R agonist confirming that antagonist induced blocking of IgM secretion is via CB2R. They also showed that transcription factors including Bcl6, PAX5, XBP-1, NF-kB and STAT were involved in the regulation of IL-6 induced IgN expression by CB2R antagonist.

B-lymphocytes express highest levels of CB2R mRNA among all the leukocytes. Very little is known about effects of CB2R modulation in B-lymphocytes on differentiation and function. The authors tried to investigate the modulatory activity of CB2R antagonist and inverse agonist on a human B cell line.

Major concerns of the present study are

(1) the purpose and rationale of the study is not explained well,

(2) why the antagonist or inverse agonist were employed to investigate the CB2R modulation in B cell line? Is there any therapeutic implication to the particular study?

(3) What is the effect of CB2R agonist on the B cell line?

(4) In Figure 2 it is claimed that CB2R agonist reverses the inhibitory effect of the inverse agonist, but the inhibitory effect does not look very significant. There are no statistical analyses included.

(5) Although, the agonist has been used to block the effects of the antagonist to prove that antagonist’s effect on IgM suppression is through the CB2R, the direct effect of the agonist is not discussed, as agonist are also known to modulate/inhibit NF-kB pathway.

(6) G-protein couples receptor ligands work through MEK/ERK. IL-6 may not have any effect on MEK/ERK in inducing IgM in SKW 6.4 cells, however, the inhibition by inverse agonist may involve MEK/ERK which hasn’t been studied using the inhibitors.

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