

3 June 2015

Dear Editor

Please find enclosed the edited manuscript in Word format - file name: 18255-revised (unmarked).

**Title:** Immune dysfunction in acute alcoholic hepatitis

**Authors:** Ashwin Dhanda, Peter Collins

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript No:** 18255

Thank you for accepting our manuscript "Immune dysfunction in acute alcoholic hepatitis" for publication in World Journal of Gastroenterology subject to minor revision.

We appreciate the comments of both reviewers and would like to take this opportunity to address them point by point.

1. The format has been updated as per the editor's recommendations
2. Reviewer 1 suggested inclusion of discussion of the use of G-CSF for the treatment of AAH. We agree this was an important oversight in the original manuscript and have included a separate sub-section to discuss the relevant data regarding G-CSF.
3. Reviewer 2 suggested some minor changes which have been made:
  - a. Glucocorticoids are not only immunosuppressive – this has been altered to "immuno-modulatory"
  - b. Treatment of AAH was not with tumour necrosis factor alpha but tumour necrosis factor alpha antagonists – this has been altered
4. Reviewer 2 suggested inclusion of trial data regarding anti-TNF therapies and this has now been included in the introduction including the references suggested.
5. Reviewer 2 has highlighted that Kupffer cells are the main contributory immune cell to the inflammatory cascade and that the term Kupffer cells and hepatic macrophages are synonyms. We agree that tissue resident hepatic macrophages (Kupffer cells) are the principal driving factor for inflammation in AAH in response to TLR stimulation. However, we prefer the more general term hepatic macrophages to also include infiltrating monocytes that mature to macrophages. Although this is likely to be a small subset of hepatic macrophages we feel their contribution to the inflammatory cascade should not be overlooked. As suggested we have specifically included Kupffer cells in the discussion of PAMP stimulation of innate cells and also emphasised that they are the main cell type that is involved.

Thank you once again for publishing our manuscript in the World Journal of Gastroenterology.

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