

August 17, 2013

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: Paper for WJS, ID: 00503431).

**Title:** Set-up of a new immune-based model of IBD in rats to study the complex steps of autoantibodies in the pathogenesis of IBD

**Author:** Hadi Esmaily, Yara Sanei, and Mohammad Abdollahi

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

**ESPS Manuscript NO:** 4423

The manuscript has been carefully improved according to the suggestions of reviewers:

1. Format has been updated
2. Revision has been made according to the suggestions of the reviewer but please be noted that:
  - a. It needs more studies to clarify whether this model present pathological aspects of CD or US, but as we suggest in the text, UC is much more related.
  - b. It needs more studies to define whether 5-ASA is efficiently control the inflammation of this model or not. This has to be tested. This is a hypothesis article.
  - c. We are not going to treat IBD in this study, our point is to ascertain our hypothesis and setting up a novel model with similar characteristics of human IBD

Reviewer 1 (00506590):

This manuscript present an interesting hypothesis to explain the development of IBD. I could not see the figures associated with this work and that limits my ability to review this work.

Answer: Thanks,

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Reviewer 2 (00742314):

The manuscript aimed “to present a new hypothesis to distinguish the complex links between genetic susceptibility, barrier dysfunction, commensal and pathologic microbial factors and inflammatory response especially autoantibodies in the pathogenesis of IBD”. The text is very well-written, understandable and raise a very elegant new hypothesis. I strongly recommend its publication .

Answer: Thanks many.

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Reviewer 3 (00506532)

Very interesting paper, whereas all the research in IBD and Crohn's disease is focused on attenuated but viable pathogens and commensals (see Review Martin et al on the Role of commensal and probiotic bacteria in human health: a focus on inflammatory bowel disease). This work uses just simply heat-killed commensal bacteria. The effect of the heat-killed commensal bacteria in providing protection is astonishing. The work and animal model presented by Abdollahi et al., certainly opens new possibilities to study chronic inflammations of the intestine. Why are great ideas often so simple? My complements to the authors! Unfortunately the work requires still a great deal of language polishing, although reviewed by others, and commented by the authors, i.e. Escherichia is still written as Eshirshia. This is the only but in my opinion still an important part in the paper that requires attention.

Answer: Thanks, The Eshirshia was replaced with Escherichia.

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Reviewer 4 (02445239)

This hypothesis is not adding anything new to the existing literature about IBD and not suitable for World journal of gastroenterology.

Answer: Thanks, although the novelty of the hypothesis has been stated in the article, the respected reviewer can read the followings:

- 1) Specific antibodies such as pANCA, anti-lymphocytes, anti-goblet cell, pancreatic autoantibodies have any role in the pathogenesis of IBD or there are only serological responses.
- 2) To specify difference between UC and CD in the role of these specific antibodies?
- 3) To identify why patients with IBS are more susceptible to being diagnosed with IBD? And what is the relation between increasing the permeability of enteric barrier and susceptibility to IBD.

History of science demonstrated that lots of our findings about pathogenesis and treatment of disorders obtained when new animal models set up. Although there are some animal model of IBD, however this model is not expensive, producible and more similar to human IBD when compared with TNBS, Dextran and other mucosal irritants.

In this regard World Journal of Gastroenterology which is founded to publish papers on the edge of gastroenterology is the best candidate for such new investigations, and we are hopeful that this model will be popular soon and this paper will be cited with other investigators.

3. References and typesetting were corrected.
4. Also be noted that one of reviewers had made wrong points related to our previous paper! (wrong review)
5. Thanks to the rest of reviewers who accepted article as it is.

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

Sincerely yours,

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