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**Commentary: associations between immune activation,
intestinal permeability and irritable bowel syndrome -
author's reply.**

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AP&T invited commentary by Jovani et al. - authors' reply

Jovani et al. October 2012

- . heightened immune activation in IBS + higher intestinal permeability
 - . non-inflammatory factors such depression/stress might influence the immune system
 - . inflammation cause or consequence?
 - . immune system + integrity of IEB but role of brain-gut axis?
- >role of gut microbiome and small intestinal bacterial overgrowth (SIBO) + potential benefits of probiotics and rifaximin

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- (i) The "Manuscript Type" should be entered as "Invited Commentary"
 - (ii) When entering a title, please begin this with "Reply to Invited Commentary: Associations between immune activation, intestinal permeability and irritable bowel syndrome" – in this way we can ensure it is associated with the original commentary.
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Manuscript Type: Invited Commentary

Reply to Invited Commentary: Associations between immune activation, intestinal permeability and irritable bowel syndrome

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Abstract: None required

We thank Dr. Jovani and colleagues for their comments regarding our review on associations between irritable bowel syndrome (IBS) and gut inflammation.

Many studies have assessed inflammatory markers in IBS and yielded a considerable amount of heterogeneous data, which made the link between IBS and inflammation difficult to evaluate. Thus, the aim of our review was to clarify this link by determining if the levels of inflammatory markers in fecal samples, blood samples or intestinal biopsies were higher in IBS patients than in healthy controls.

Other risk factors such as stress and psychological factors are involved in IBS etiology¹, however these were not described in detail since this was out of the scope of the present review. We also fully agree that alteration of the gut microflora can contribute to IBS etiopathogenesis. Actually, dysbiosis was quite consistently reported in IBS.² Small intestinal bacterial overgrowth (SIBO) has been somewhat associated with IBS³ although the existence of a causal link between IBS and SIBO is still under debate because most of the existing studies are methodologically biased or lack the appropriate controls.⁴

In line with a possible involvement of dysbiosis and/or SIBO in IBS, recent studies have shown beneficial effects of the antibiotics mesalazine and rifaximin on symptomatology.⁵ Probiotics can relieve symptoms in some cases as well.⁶ Nevertheless, large randomized and controlled trials are still needed to further evaluate the effectiveness of anti-inflammatory agents and probiotics for treating IBS. Associations between beneficial effects of antibiotics and presence of SIBO are lacking as well.² Despite these shortcomings, modulation of the intestinal flora could indeed be a prosperous direction of future research. The pathophysiological

consequences of these microflora changes in IBS are not well understood. However, one explanation could be the increase in intestinal permeability following alteration of tight junction complexes in intestinal epithelial cells and subsequent immune activation within the mucosa.⁷

Acknowledgement: The authors' declarations of personal and financial interests are unchanged from those in the original article.⁸

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