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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 6419
Title: Combined Probiotic Bacteria Promotes Intestinal Epithelial Barrier Function and Tight Junction Expression in IL-10 KO Mice
Reviewer code: 00007966
Science editor: Cui, Xue-Mei
Date sent for review: 2013-10-18 15:05
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The aim of this animal study was to determine whether combinations of probiotic (Bifico) can decrease severity of colitis in IL-10 gene-deficient (IL-10 KO) mice, and inflammatory response in Caco-2 cell monolayers exposed to E.Coli. The authors report that oral administration of Bifico [approximately 1.5×108 colony-forming units (CFU) per day of Bifico] for four weeks. Decreased severity of colitis in IL-10 Ko mice; but the data presented showed that even those mice that received Bifico still had rather significant inflammation of their colon. Bifico almost completely prevented gut leakiness in IL-10 Ko mice [Ussing chamber]. Treatment of Caco-2 monolayers with Bifico or single-strain probiotics in vitro inhibited EIEC invasion and reduced the secretion of pro-inflammatory cytokines. The authors concluded that oral administration of Bifico reduced colon inflammation in IL-10 KO mice, and directly promoted epithelial barrier function in both in vitro and in vivo models. I have a few comments and questions. 1. Introduction. Authors should avoid use of IBD and simply use "colitis". IL-10 Ko model only some aspects [colon inflammation] of IBD. 2. Result. It is stated that figure 2 B showed only mild cell infiltration and mucosal damage. How did you define "mild"? It should be noted that histogram showed that mice treated with Bifico still had colitis score of 5 [untreated IL-10Ko mice score was just above 6] thus the colitis in treated IL-10 mice is still rather significant and is not "mild". Similarly drop in TNF and IFN [figure 2] is partial and the levels of these two cytokines in treated IL-10Ko are still substantially high and are over 2 folds above the control values. It should also be noted that treated IL-10 Ko mice still had significant lower weight than WT mice [figure 1]. This point that the effects of Bifico on colonic inflammation was partial and treated mice still had evidence of substantial inflammation should be highlighted in

abstract and discussed in the Discussion section.

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[Y] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[Y] Accept
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COMMENTS TO AUTHORS
The authors have performed a very good study of improving gastrointestinal mucosal biology in a colitis-like model. I have a few comments/suggestions for them to consider: 1. In the abstract (pg 3) mention that Bifico is given orally by gavage. 2. In the Discussion, discuss how probiotic microbes "survive" gastric acidification and digestion. 3. The authors need to describe (pg 8 and elsewhere)whether the IL-10 mice used here (normally kept in germ-free conditions) were removed from germ-free conditions as part of the experimental protocols. Do they not have to be in normal (germ) conditions to develop symptoms? The authors need to say yes or no to this in the manuscript. 4. On page 11, the authors state using 3 micron pore filters to support the CACO-2 cells. Know that 3 micron is a poor choice, as cells are capable of extrusion through 3 micron pores. 0.4 micron is better. 5. The authors never state whether EIEC and also the probiotics are placed on BOTH sides of the CACO-2 cell layers. Please define. 6. I would not use the term "IBD" to describe the IL-10 mice. Better to say "colitis-like condition." 7. The authors state that probiotics are supplied to the CACO-2 cells for only 30 minutes before EIEC. The authors should discuss what can happen to/change in the CACO-2 cell layers in only 30 minutes that can protect them froim the EIEC. Is it only competition for extracellular receptors such as TOLL ? 8. The authors never say if cell DEATH is being caused by the EIEC. Is it? 9. In Figure 5 I was surprised to see 1250 ohm resistances for CACO-2. These are very high resistance values. Minor Comments: 1. On page 9, define VCC MC8. Is this a manufacturer? 2. Page 5, paragraph 2: change "often induces" to "occurs with" 3. Page 4: change "ameliorated" to "improved"