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ESPS Peer-review Report
Name of Journal: World Journal of Gastrointestinal Pathophysiology
ESPS Manuscript NO: 9275
Title: Adherent invasive E. coli in Crohn's disease and other intestinal disorders
Reviewer code: 00009417
Science editor: Huan-Huan Zhai
Date sent for review: 2014-02-08 09:50
Date reviewed: 2014-02-11 01:55

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS
In the review the focus is given on E. coli strains in the pathogenesis of intestinal disorders including Crohn's disease. The review could be improved by a scheme demonstrating the impact of E. coli on IBD.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastrointestinal Pathophysiology
ESPS Manuscript NO: 9275
Title: Adherent invasive E. coli in Crohn's disease and other intestinal disorders
Reviewer code: 00188382
Science editor: Huan-Huan Zhai
Date sent for review: 2014-02-08 09:50
Date reviewed: 2014-02-12 05:31

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

Dear Editor-in-Chief, Thanks for inviting me to review the manuscript titled: "Adherent invasive E. coli in Crohn's disease and other intestinal disorders". The topic is interesting, and I am presenting some major concerns that need to be address in order to consider this manuscript acceptable for publication. Major concerns: 1. The title mention: "…. in Crohn's disease and other intestinal disorders". Due to the fact that authors performed an extensive review on ulcerative colitis (UC) as well as in celiac disease, but not in other intestinal diseases like –for example- irritable bowel syndrome or intestinal infections, I think it will be more appropriate to restrict the title to:" ……in chronic inflammatory bowel diseases". 2. In the abstract authors claimed: "we present the latest research findings concerning AIEC host-microbe interactions and pathogenicity." In this regard, only information regarding the potential role of TLR-5 in intestinal epithelial cells and AIEC was presented. However, authors should review the role of other pattern-recognition receptors (PPR) involved in bacterial antigen recognition such as TLR-2, 4, 6 as well as any potential involvement from additional PPR like Nod-1 and 2, knowing the fact that there are Nod polymorphic sequences strongly associated with Crohn's disease. Moreover, bacteria antigen up-take in the interface at the intestinal epithelial barrier, including Peyer's patches, can be driven by mucosal dendritic cells. However, little information about this cells type and intestinal pathophysiology in IBD has been presented in this review. Therefore, this particular topic needs to be address in more detail. 3. Authors presented a good review showing that there is an altered intestinal microbial community in IBD characterized by an increase in E. coli. However, this imbalance can be a consequence of a primary exacerbated inflammatory response and liking intestinal epithelial barrier. Can authors

review and discuss this point in order to understand which could be the potential pathophysiological relevance of this E coli imbalance in the pathogenesis of IBD? 4. Authors stated:" On average, in our cohort, E. coli 16S rRNA gene copies accounted for 14% and 33% of total bacteria 16S rRNA gene copies in healthy subjects and ileal CD patients, respectively ($p<0.001$)." However, reference is missing. Please provide reference and check that after every statement there is a reference supporting the idea presented. 5. Authors presented information about the controversy in UC, explaining few factors that may explain why there is no clear consensus about an imbalance of E. coli in this clinical setting. However, authors omitted to discuss the different methodologies used to detect E. coli in UC and the potential implications of this factor in research outcome. Can authors review this point providing a detailed analysis of this factor as well? 6. At some point during the review authors presented the following information: "A novel mechanism of pathogenicity observed in LF82 and two other AIEC strains (O83:H1 and UM146) is the evasion of host immune responses via subversion of the IFNγ pathway in intestinal epithelial cells[58]. Phosphorylation of the Signal Transducer and Activator of Transcription STAT-1 is blocked, thus preventing the transcription of IFNγ-dependent genes, which reduces host immune responses and results in an inability to mount an appropriate anti-microbiocidal response." However, this mechanism and others can be part of a common physiological response towards most of the intestinal microbiota in order to create a tolerogenic environment, avoiding any host immune response. Have authors review if this is the case for other commensal bacteria from the gastrointestinal track? It is also important to put in perspective that a physiological transit of commensal bacteria exits between the intestinal lumen, Peyer's patches, and mesenteric lymph nodes, which is essential