

## ESPS Peer-review Report

**Name of Journal:** World Journal of Gastrointestinal Pharmacology and Therapeutics

**ESPS Manuscript NO:** 2177

**Title:** Inflammatory Bowel Disease: an archetype disorder of outer environment sensor systems

**Reviewer code:** 01115220

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-02-04 20:18

**Date reviewed:** 2013-02-26 16:55

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

In this paper the authors have made an argument that the classical IBDs should be viewed as part of a spectrum of diseases with failed environmental sensing. This is certainly an interesting idea and I think does deserve further scrutiny. Whilst many ideas and discussions in the paper are sound, I feel that as a whole the paper rather lacks focus and structure. The paper would be much stronger if the introduction laid out what the thrust and argument of the paper was going to be and how the authors were going to link this to other diseases: as it stands the additional and interesting text about non-GI diseases, seems rather appended to an otherwise standard review of current concepts of IBD pathogenesis. With some careful restructuring and a more transparent linear hypothesis running through the paper, this manuscript would stimulate useful discussion. Specific other points: 1. Page 2, line 5, the the discussion of the CARD15 variants does not make sense. 2. Page 2, line 10, presumably the authors mean IKappaB here? If so why not explain this specifically? 3. Page 2, 3 lines from bottom, I do not think it is the ATG16-L1 gene that is recruited to the membrane, presumably the gene product? 4. Page 3, line 9, do the authors really mean that STAT6 signals through IL-13, surely IL-13 signals via STAT6? 5. Page 7, the interesting data concerning the Crohn's-psoorisis overlap, lack references. 6. Given the authors' overall hypothesis about a collection of diseases with failed environmental sensing, I think the discussion about COPD is rather too brief. This might be an interesting insight but given that smoking is by far the most important risk factor for COPD, how do the authors relate failed environmental sensing to the pathogenesis of COPD? 7. The paper really does gloss over the failure to detect NOD2 mutations in significant Crohn's populations (page 8), given the central thrust of the paper, I do feel some attempt to explain such apparent anomalies is required.

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**Title:** Inflammatory Bowel Disease: an archetype disorder of outer environment sensor systems

**Reviewer code:** 00503072

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-02-04 20:18

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

In general, this is a nice and necessary review. In this review, the authors summarize the update knowledge of environment-host interaction in the development of IBD, and discuss the role of disorder of environmental factors during the inflammation processing, which may provide the important understanding information to the readers.