

## PEER-REVIEW REPORT

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

**Manuscript NO:** 34724

**Title:** The intestinal epithelium, intraepithelial lymphocytes and the gut microbiota – key players in the pathogenesis of celiac disease

**Reviewer's code:** 01944824

**Reviewer's country:** United States

**Science editor:** Yuan Qi

**Date sent for review:** 2017-05-23

**Date reviewed:** 2017-05-24

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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 type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

## COMMENTS TO AUTHORS

Lines 30-31: The implication here is that gluten appears in genetically predisposed individuals.

Line 33: Use “deamidated” only once in a sentence.

Line 65: see lines 30-31

Line 67: Delete “It is known that”

Lines 82-85: Run-on sentence

Line 86: Delete “It is known that”

Lines 95-97: Please reference. The introduction of gluten by 17 weeks of age is not universal. Nevertheless, recent data suggest the CD risk may be increased in subjects delaying gluten exposure until after one year of age. The authors must consider this phenomenon in their exposition.

Lines 156-157: The authors should be more descriptive in discussing the zonulin pathway. Increased permeability (via paracellular movement) is induced by the opening

of tight junctions, thus permitting macromolecular uptake.

Line 162-170: How does a polarity change influence permeability? The unfortunate implication here is that the Dutch study represented a population of genetically unique (and homogeneous) subjects. While the study was performed in the Netherlands, I doubt whether this conclusion was either stated or implied. Please re-write, with special attention to grammar and sentence structure.

Lines 213-221: Poorly written, difficult to interpret, with run-on sentences. The last sentence is unintelligible. Please review and re-write.

Lines 227-228: This statement is incorrect. The microbiota:cell ratio is much closer to 1:1 (Sender R, Fuchs S, & Milo R. (2016) Revised estimates for the number of human and bacteria cells in the body. bioRxiv doi: <http://dx.doi.org/10.1101/036103>)

Lines 385-388: Please clarify the risk determination in these situations (?increased, ?decreased).

Lines 391-397: Please re-write. This is extremely confusing and difficult to interpret. The authors must be careful in implying that the HLA DQ2/DQ8 genotype “found in CD patients” is associated with a specific microbial fingerprint. Since 25-30% of the general population exhibits the same HLA alleles, other factors must be prescient (assuming the microbial population in CD is unique).

Lines 405-411: Convoluting, run-on sentences, without a clear focus. Furthermore, data either “suggest” or “may indicate” (the term “could suggest” is not acceptable).

Concluding Remarks: If this reviewer has interpreted the manuscript correctly, the authors are stating the following:

Patients with latent CD manifest a unique microbial fingerprint. This “CD specific” distribution of microbial species is likely dependent upon specific genetic factors, including (but not exclusively) the HLA DQ2/DQ8 phenotype. Under conditions of altered gut permeability, for example during acute infection, macromolecular uptake (via the opening of paracellular tight junction gates, cf. Fasano et al) leads to translocation of dietary macromolecules and microbial elements. This phenomenon triggers a cascade of events in genetically susceptible individuals, leading to overt CD.

At least, that is my reading of this section, which must be rewritten to address: 1. A review of data presented and the derived conclusions; and, 2. A suggested pathway for future research.

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**Manuscript NO:** 34724

**Title:** The intestinal epithelium, intraepithelial lymphocytes and the gut microbiota – key players in the pathogenesis of celiac disease

**Reviewer's code:** 01552044

**Reviewer's country:** Italy

**Science editor:** Yuan Qi

**Date sent for review:** 2017-05-23

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

This is an interesting and comprehensive manuscript dealing with the immunological aspects underlying celiac disease. In my opinion it only needs to be reviewed by an English speaking person before it is accepted for publication

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

**Manuscript NO:** 34724

**Title:** The intestinal epithelium, intraepithelial lymphocytes and the gut microbiota – key players in the pathogenesis of celiac disease

**Reviewer's code:** 00343118

**Reviewer's country:** Italy

**Science editor:** Yuan Qi

**Date sent for review:** 2017-05-23

**Date reviewed:** 2017-06-01

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input type="checkbox"/> High priority for publication
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		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

A comprehensive and critical view of the relevant literature regarding Celiac disease pathogenesis, and in particular on the role of microbioma in the alteration of the gut epithelial barrier.