PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 65682

Title: Antimicrobial Peptides and the Gut Microbiome in Inflammatory Bowel Disease

Reviewer's code: 03254190

Position: Peer Reviewer

Academic degree: PhD

Professional title: Senior Researcher, Senior Scientist

Reviewer's Country/Territory: Norway

Author's Country/Territory: United States

Manuscript submission date: 2021-03-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-03-20 16:01

Reviewer performed review: 2021-03-30 11:24

Review time: 9 Days and 19 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In the Frontier article: Antimicrobial Peptides and the Gut Microbiome in Inflammatory Bowel Disease, Gubatan et.al., present an overview of the major classes of AMPs in the Gastrointestinal tract (Table 1), results from functional studies of AMPs in preclinical models (Table 2) and studies of Biomarker applications of antimicrobial peptides in patients with IBD (Table 3). The review is nice and compact. However, the manuscript includes some structural problems and confusing descriptions.   In general, it would be useful to clarify where the data described were generated in animal models or cell lines, since it is often not obvious whether the authors are discussing human data or rather studies in e.g., rodents.   Are there differences in distribution and regulation of AMPs in pre-clinical animal models compared to humans?   In the main text, I think information in the sections "Antimicrobial peptides in the Gastrointestinal" tract and "Antimicrobial Peptides and Gut Microbiome" will appear less repetitive if the authors merge description of the different AMPs.   The authors should avoid including many reviews by others as references (e.g., refs 5, 8, 14, 40, 41, 42, 43, 44, 46, 47, 48, 60, 68, …78, ++), or at least explain why they are included in the present review.   Specific comments: Table 1: Antimicrobial peptides in the Gastrointestinal Tract. Description of tissue expression, location and cellular origin can be clearer. The precision level (i.e., Paneth cells, enterocytes of small and large intestine, colonic epithelial cells, Enterocytes, Epithelial Cells, Intestinal Epithelial Cells) appears somewhat random? What is the rationale for including studies of epithelia in human lung (ref 15), mast cells in skin (ref 17)?   Studies in animal models or cell lines like Caco2 and HT29 should be separated from studies in IBD-patients. I also suggest including some references from human studies for all AMPs.   Table 3: I would recommend that the authors consider including some recent publications like "Faecal Biomarkers in Inflammatory Bowel Diseases: Calprotectin Versus Lipocalin-2-a Comparative Study" PMID: 32556317

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

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Title: Antimicrobial Peptides and the Gut Microbiome in Inflammatory Bowel Disease

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Reviewer's Country/Territory: Brazil

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Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In this review/frontier article, the authors "discuss the function and mechanisms of AMP in the gastrointestinal tract, examine the interaction of AMP with the gut microbiome, explore the role of AMP in the pathogenesis of IBD, and review translational applications of AMP in patients with IBD." The authors make an elegant review of the literature, defining the biomarkers and even showing their clinical applicability. Calprotectin is the most widely used biomarker in clinical practice. Despite its routine use in clinical practice, there is still no well-established cut-off value for classifying patients in activity or remission of the disease. I suggest that the authors discuss the cut-off values of calprotectin in the differentiation between active disease versus remission, as well as whether there are established calprotectin values to determine therapeutic response to any medication, such as a drop of x% from the initial value, for example.

PEER-REVIEW REPORT

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Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The review by Gubatan et al. is a good manuscript but before this review is published I request that a paragraph on arachidonic acid metabolism in relation to the function and mechanisms of AMPs in the Pathogenesis of IBD be written. Indeed, the expression and activity of COX-2 is important in inflammatory bowel diseases as well as pro-inflammatory cytokines (IL-1, TNFa) that induce COX-2. Also in the "Donkey Milk Lysozyme" section, to my knowledge IL-13 is not a pro-inflammatory but an anti-inflammatory cytokine. This aspect needs to be corrected or better written.