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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 34197
Title: Expression of Interleukin-26 is upregulated in inflammatory bowel disease
Reviewer's code: 03476711
Reviewer's country: Egypt
Science editor: Ya-Juan Ma
Date sent for review: 2017-04-10
Date reviewed: 2017-04-15

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[Y] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[Y] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Dear authors very interesting meticulous study.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 34197
Title: Expression of Interleukin-26 is upregulated in inflammatory bowel disease
Reviewer's code: 02545516
Reviewer's country: Germany
Science editor: Ya-Juan Ma
Date sent for review: 2017-05-10
Date reviewed: 2017-05-13

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In their report "Expression of Interleukin-26 is upregulated in inflammatory bowel disease" Makoto et al. present relevant novel data on the potential role of the Th17 Interleukin-26 in inflammatory bowel disease. In extensive and robustly performed set of experiments the authors rise several novel findings: IL-26 upregulation in both IBD subtypes (CD>UC), expression of the respective IL-26 receptor complex on cultured human colonic subepithelial myofibroblasts (SEMF), induction of inflammatory mediator secretion upon IL-26 stimulation and elegantly performed mechanistic experiments concerning IL-26 signalling resulting in NF-kB/AP-1 activation. Overall, the study presents novel data in a relevant research topic. Some minor points, however, should be addressed to improve the paper: 1. Prior treatment effects may impact on cytokine studies and have not been mentioned in the paper. So the Authors are advised to include IBD treatments, in particular immunosuppressive and anti-TNF 2. myofibroblasts are typical fibrogenic cellular players; it would be tempting to speculate that SEMF activation by IL-26 may pave the way for enhanced fibrosis, e.g. setting the

stage for stricturing Crohn´s disease – the Authors should elaborate on this topic in the discussion 3. Comparison of surgical vs. colonoscopic biopsies may introduce significant bias in the study (different cellular sources, different levels of inflammation, etc.) – this should be critically discussed in the manuscript.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
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Reviewer's code: 00503628
Reviewer's country: United States
Science editor: Ya-Juan Ma
Date sent for review: 2017-05-10
Date reviewed: 2017-05-17

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The manuscript by Fujii and colleagues examines the production of IL-26 during inflammatory bowel disease (IBD). IBD includes two major types, Crohn's disease (CD) and ulcerative colitis (UC) both of which reflect dysregulated immune responses to gut flora. However, both diseases differ in areas which are affected and the type of response. The focus of the manuscript is to describe the production of IL-26 in IBD. The first figure demonstrates an elevated expression of IL-26 mRNA in biopsies of patients with active disease, which was significantly higher in patients with CD than UC. However, the results from figure 1 are not confirmed by the immunohistochemistry results (Figure 2A), which shows marked expression of IL-26 in the mucosa of UC patients. In fact, the staining suggests the presence of more IL-26+ cells within the UC mucosa. The results in figure 2B confirm multiple cell phenotypes expressing IL-26. The authors then proceeded to examine IL-26 (IL-20R1 or IL-10R2) receptor expression, which is abundant in the mucosa during active UC, but these results fail to provide evidence of IL-26 receptors in the normal, CD or inactive IBD. Thus, it is difficult to make comparisons or

clear statements regarding this expression. Again, it is interesting why the authors do these studies with UC samples while the first set of results provided showed a "significantly higher expression of IL-26 mRNA in CD than UC". It is also not clear why on Figure 4 they focused on SEMFs when their results suggest that these cells represent a minor population of IL-26 receptor positive cells in the mucosa. The intracellular signaling studies suggest that all pathways examined are involved. Basically, all inhibitors tested had a suppressive effect. STAT1/3 and MAPKs/PI3K as well as NF-κB/AP-1 are activated by IL-26. Perhaps the authors could have presented a diagram depicting the pathways activated. The only difference from previous studies is the use of SEMFs rather than epithelial cells, which represent the most abundant cell type expressing IL-26 receptors, as shown by the authors data in Figure 4.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
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Title: Expression of Interleukin-26 is upregulated in inflammatory bowel disease
Reviewer's code: 03646676
Reviewer's country: Italy
Science editor: Ya-Juan Ma
Date sent for review: 2017-05-10
Date reviewed: 2017-05-21

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[Y] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[Y] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The present manuscript from Fujii et al. is interesting and well written. Data are abundant and solid and provide insights to IL-26's role in intestinal inflammation

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 34197
Title: Expression of Interleukin-26 is upregulated in inflammatory bowel disease
Reviewer's code: 03252972
Reviewer's country: China
Science editor: Ya-Juan Ma
Date sent for review: 2017-05-10
Date reviewed: 2017-06-06

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[Y] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
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[ ] Grade E: Poor		[Y] No	[ ] Major revision
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		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The authors demonstrated that an increased expression of IL-26 in the inflamed mucosa of IBD patients and explored its possible pathway in IBD pathology. The study is well designed and the demonstration seems sufficient. However, from a clinical point of view, several questions still remain unclear. I would suggest authors either add some further experiments or address them in the discussion. 1. What is the reason of the increase of IL-26? 2. The association between IL-26 and IBD is covered in the study, but whether this association is decisive is not yet determined. Effect of inhibition of IL-26 or its pathway is not studied in the current paper. 3. Following the above question, what is the clinical importance or application of the findings of this study?