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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 6564
Title: Differential Expression of IL-1/TLR Signaling Regulators in Microscopic and Ulcerative Colitis
Reviewer code: 01429233
Science editor: Ma, Ya-Juan
Date sent for review: 2013-10-25 17:40
Date reviewed: 2013-12-18 17:57

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] 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:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
MS ID: WJG 20131023195144 Title: DIFFERENTIAL EXPRESSION OF IL-1/TLR SIGNALING REGULATORS IN MICROSCOPIC AND ULCERATIVE COLITIS By Dr. Sezin Günaltay, and colleagues. Comments for the authors 1. The Mayo's scoring system presented in the Table is unnecessary, already widely known. 2. Number of cases in subgroups is very small, and this may compromise the validity of the findings for a global readership to apply. This is particularly serious with regard to collagenous colitis histopathological remission. 3. The manuscript should benefit from language editing by one of the co-authors with clinical experience within the scope of this manuscript.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 6564
Title: Differential Expression of IL-1/TLR Signaling Regulators in Microscopic and Ulcerative Colitis
Reviewer code: 00158526
Science editor: Ma, Ya-Juan
Date sent for review: 2013-10-25 17:40
Date reviewed: 2014-01-03 00:15

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] 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	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS
General comments: this is a very nice study about expression of the cytokines in the GUT in ulcerative colitis and microscopic colitis. Specific Comments: Discussion: Is very well organized. References: Are appropriate, relevant, and updated. Tables and figures: Are appropriate, well structured. Therefore I classified the manuscript Differential Expression of IL-1/TLR Signaling Regulators in Microscopic and Ulcerative Colitis into grade B. According to the language evaluation the revised article is evaluated as grade B. I conclude that the authors should make only minor changes in the article regarding English language, so I think that you should accept it.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 6564
Title: Differential Expression of IL-1/TLR Signaling Regulators in Microscopic and Ulcerative Colitis
Reviewer code: 00061704
Science editor: Ma, Ya-Juan
Date sent for review: 2013-10-25 17:40
Date reviewed: 2014-01-08 19:18

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[Y] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[Y] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] 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	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
The authors compared the expression s of Il-1/TLR signaling regulators (IRAK-2, IRAK-M. IL-37 and nicroRNAs (miR 146, -155 and -21 in colonic biopsies obtained from patients with microscopic colitis (MC) and ulcerative colitis (UC). The identification of differentially expressed miRNAs, IL-37 and IRAK-M suggest that colagenous colitis and lymphocytic colitis are different clinical entities. In my opinion it is interesting and very original study sheding a new light on the pathophysiology of MC. The only limitation is the low number of patients included in this study.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 6564
Title: Differential Expression of IL-1/TLR Signaling Regulators in Microscopic and Ulcerative Colitis
Reviewer code: 00068090
Science editor: Ma, Ya-Juan
Date sent for review: 2013-10-25 17:40
Date reviewed: 2014-01-09 01:04

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] 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	[Y]Rejection
[Y] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The authors present a differential expression of IL-1/TLR regulators in microscopic and ulcerative colitis. The major objection of this study is the low number of patients that involves to the results presented and for this reason do not provide sufficient experimental evidence or data to draw firm scientific conclusions: 1) The authors should consider in their discussion and conclusions the frequent association of LC with other autoimmune disorders (thyroid disease, diabetes mellitus, celiac disease, psoriasis, and rheumatoid arthritis), inflammation in the lamina propria with increased intraepithelial lymphocytes and the fair response to steroids. In this sense infectious agents, drugs, or food antigen such as gluten may be precipitating factors 2) The authors should more data about if they noted complete histological and/or symptomatic remission in the patients and also if there is other patients that reverted back into UC , because others authors suggesting that LC could present as a continuum of UC. Are the patients completely asymptomatic? 3) The induction of IRAK-M is necessary to limit pathologic inflammation and cytokine secretion. The authors should consider that IRAK-M has varying roles in immunopathology depending on the disease context. For example, in the setting of chronic inflammatory diseases, IRAK-M expression is desirable because it can limit excessive immune responses. In contrast, IRAK-M expression may prevent proper innate immune clearance of pathogens in the setting of immunodeficiency. Moreover, deficiencies in IRAK-M may predispose individuals to inflammatory bowel disease (IBD), as IRAK-M is on the genetic susceptibility locus for IBD. In ulcerative colitis patients, an association between caspase recruitment domain (CARD15) mutant patients and IRAK-M was found, suggesting a possible impairment in the negative regulation of TLR-signaling causing IBD. IRAK-M has a well-established role in reducing immune responsiveness to continuous pathogen exposure. By negatively regulating TLR signaling,

IRAK-M inhibits production of pro-inflammatory mediators and contributes to the induction of endotoxin tolerance 4) The authors should better explain and interpret the results obtained. In this sense what it is the significance the increased expression of miR-155 in active UC, active CC and LC in remission? . What is the interpretation the enhanced expression of miR-21 (anti-inflammatory) in active CC, but no in remission and increased in LH remission but no in active?. 5) How is possible that in active CC, active UC and LH in remission patients present increased expression of miR-155 and increased expression of miR-21, if the up-regulation of miR-21 decrease miR-155 expression? 6) The discussion should rewritten, in which interpret and discuss better the results obtained .

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
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Title: Differential Expression of IL-1/TLR Signaling Regulators in Microscopic and Ulcerative Colitis
Reviewer code: 00503587
Science editor: Ma, Ya-Juan
Date sent for review: 2013-10-25 17:40
Date reviewed: 2014-01-10 04:56

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	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

The manuscript by Gunaltay and colleagues focuses on key TLR regulators in colitis. Overall comment: The conclusions able to be clearly drawn from this work is limited by the small samples sizes, and the bias from variations within each subgroup (esp. treatment effects). These limitations must be more clearly acknowledged Specific Comments 1. There are minor errors of english grammar and/or sentence construciton that require correction 2. The word MACROSCOPICALLY is used incorrectly in at least three places in the manuscript. This should be corrected to read endoscopically (as macroscopically refers to examination with the naked eye). 3.Crohn disease was an exclusion factor for the patient groups. Was this excluded just on the basis of colonoscopy or was upper endoscopy and small bowel imaging also completed to definitively exclude CD? 4.In the methods section (page 5), the text reports that patients diagnosed with MC underwent tests because of three symptoms. This implies thatr all patients had all three symptoms - is this correct? 5. As per above comment, a number of patients were being treated with various drugs at the time of assessment: how have the authors considered the effects of these therapies? 6. Where were the study biopsies obtained? One place indicates that they were sourced from the hepatic flexure, whilst another indicates proximal colon. This should be consistent and clear. 7. Further, were the study biopsies always obtained from involved areas? (e.g. in those with UC) 8. Some of the details of the patients (as covered in Table 1) are results rather than methods, and would be better located in the Results section