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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 11114
Title: The role of IL-22 in the pathogenesis and treatment of Inflammatory Bowel Disease
Reviewer code: 00034489
Science editor: Ya-Juan Ma
Date sent for review: 2014-05-06 00:00
Date reviewed: 2014-05-21 15:11

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	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

The authors show the review of IL-22 for IBD including new knowledge. The review is well organized and has some value for specialist especially IBD researchers. There are several concerns with regards to the review. Please see below. 1) Figure 1, which is only a figure in the review, is poor quality. The figure is very important to readers. The figure should be improved to be more informative figure for readers. 2) Several paragraphs are too long. The long paragraphs should be shorten and be added subhead to read easily. 3) There are several type miss in the paper. Please check up carefully. 4) The name of several microorgasms should be written using Italic. Please check the scientific name.

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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 11114
Title: The role of IL-22 in the pathogenesis and treatment of Inflammatory Bowel Disease
Reviewer code: 00068090
Science editor: Ya-Juan Ma
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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	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

In this work the authors present a review of the role of IL-22 in the pathogenesis and treatment of inflammatory bowel disease. The authors should include the following considerations: 1) The authors should include the IL-22 function in context with other cytokines. It is important to consider the dual nature of IL-22 with respect to its protective versus inflammatory function certainly depends on a variety of factors, including the concentration and duration of local IL-22, the target tissues, and the cytokine environment. IL-22 production as well as downstream functions are influenced by cytokines such as IL-17, IL-23, IL-6, IFN-α, IFN-γ, or TNF-α. IL-22 often acts synergistically with IL-17. Data demonstrate that the precise and individual regulation of IL-17 and IL-22 production is critical to ensure an effective immune response and to avoid immunopathology. For example, the mere existence of cells expressing only IL-22 or IL-17 proves that the transcriptional control of both cytokines despite being partially overlapping is not identical. Understanding the differences in the regulation of IL-22 and IL-17 should provide insight into the physiological and pathogenic functions of these two cytokines in various diseases, as IBD. 2) The authors should include the role of Treg cells as a potential regulator for IL-22 expression in IBD. In this sense, Tregs regulate the activation and expansion of CD4+ T cells lineage, via expression of forkhead box P3 and/or their capacity to produce cytokines such as transforming growth factor (TGF)-β, IL-10, and IL-35. IL-10 antagonizes pro-inflammatory cytokines such as IL-6 and might also be an antagonist to the inflammatory IL-17.

Additionally, IL-10 negatively regulates Th17 cell differentiation.

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ESPS PEER REVIEW REPORT

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Science editor: Ya-Juan Ma
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[ ] Grade C: Good	[Y] Grade C: A great deal of language polishing	[ ] No records	
[Y] Grade D: Fair		BPG Search:	[ ] Rejection
[ ] Grade E: Poor	[ ] Grade D: Rejected	[ ] Existing	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

Previous reviews highlighted the role of IL-22 in inflammation, tissue protection, regeneration and antimicrobial defense, as well as the positive and potentially negative consequences of its therapeutic modulation (Sabat and Ouyang, 2014; Rutz et al., 2013; Mizoguchi, 2012; Gregory et al., 2011). In this review, the authors have discussed the recent progression of the involvement of IL-22 in the pathogenesis of inflammatory bowel disease as well as its therapeutic potential. In general, much of the information given in this review on the role of IL-22 in IBD pathogenesis is not novel than what had already been appeared in recent reviews (cited above). The review although highlight IL-22 as a promising target for IBD therapy, do not clarify negative consequences of its therapeutic potential. One of the suggested mechanisms that tie an intestinal dysbiosis to the pathophysiology of IBD involves the release of enteric bacterial proteases that interact with protease activated receptors on epithelial cells, resulting in intestinal barrier dysfunction and exposure of the enteric immune system to luminal antigens. (Carroll and Maharshak, 2013). In a recent review, Lin et al. (2014) focused on the regulatory role of T regulatory (Treg) cells in IL-22 expression, and studies indicated that IL-23 and several transcription factors, not only STAT3, but also RORγt, and the AhR are important stimulus in the functioning and regulation of IL-22. It would be interesting if the authors include these aspects of IL-22 regulation in Figure 1. The manuscript requires corrections for English Grammer and Style.