

**ESPS Peer-review Report**

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

**ESPS Manuscript NO:** 4686

**Title:** Longitudinal analysis of inflammation and microbiota dynamics in a model of mild chronic dextran sulphate sodium-induced colitis in mice.

**Reviewer code:** 00503405

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-16 09:16

**Date reviewed:** 2013-07-19 04:28

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

In the original article of De Fazio et al. (Longitudinal analysis of inflammation..) the authors aimed to characterize 1.5% DSS induced colitis clinically and histologically along with the changes of the colonic microbiome and systemic cytokine levels. The results of the study are of experimental merit, but there are some issues that needs revision. It is necessary to inculde into the introduction that the immunobiologic basis of DSS-induced colitis (i.e. triggering of the innate immune system) is not the same as it is in IBD (which is considered as an imbalance in adaptive immunity). The histological changes and the similarity in the changes of cytokine profiles make DSS-colitis a useful experimental model to investigate colitis. The authors underline to importance of the molecular weight of DSS in colitis induction. How was the MW of DSS in their experiment? The authors discussed that in most human IBD studies the systemic level of cytokines are measured, while in experimental colitides usually the local cytokine profile changes are examined, thus leading to information loss on systemic inflammation. As in the case of DSS-induced colitis not just DSS itself, but the gut microbiota contribute to the inflammatory process, and, moreover, some cytokines act via autocrin or paracrin pathways in a local inflammatory milieu, it would be crucial to measure not just the systemic cytokine profiles but the local cytokine profile changes. The comparison of the systemic and the local cytokine profiles would let us to take an exact insight into the immunopathogenesis of colitis. The authors did not examined the levels of type I. interferons (especially IFN-alpha and -beta). It is known that stimulation of apical epithelial Toll-like receptor 9 results in accumulation of NF-kB inhibitors, thus blocking its activation, and in suppression of inflammation, partly due to the induction of type-I IFNs. In tissue regeneration type-I IFNs are considered as protective cytokines



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against colonic inflammation. It would be crucial to know the longitudinal changes of type I. IFNs as well. Some of the changes in the observed cytokine levels may be related to the colonic microbiome and its changes. It would enhance the strength of the manuscript if the authors discussed the role of the microbiome-native immune system-cytokine profile axis in colitis induction and mucosal regeneration. The used references are up-to-date. The images/tables/illustrations all help the understanding of the results. English language needs minor revision, as well as some typos in the text must be corrected. Overall, the study is very important and has a significant experimental merit, its presentation must be improved. After major revision, I definitely suggest to accept it for publication in WJG.



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

**ESPS Manuscript NO:** 4686

**Title:** Longitudinal analysis of inflammation and microbiota dynamics in a model of mild chronic dextran sulphate sodium-induced colitis in mice.

**Reviewer code:** 00037324

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-16 09:16

**Date reviewed:** 2013-08-31 20:34

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

Minor comments: Please add parameter to x-axis for all the figures.



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### ESPS Peer-review Report

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

**ESPS Manuscript NO:** 4686

**Title:** Longitudinal analysis of inflammation and microbiota dynamics in a model of mild chronic dextran sulphate sodium-induced colitis in mice.

**Reviewer code:** 02495872

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-16 09:16

**Date reviewed:** 2013-09-26 22:31

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

Despite the fact that the DSS-induced colitis model is quite common, the authors used a state of the art approach. The paper is highly interesting and has a strong potential for being used as a benchmark for further studies evaluating possible treatments of colitis.



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### ESPS Peer-review Report

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

**ESPS Manuscript NO:** 4686

**Title:** Longitudinal analysis of inflammation and microbiota dynamics in a model of mild chronic dextran sulphate sodium-induced colitis in mice.

**Reviewer code:** 00036898

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-16 09:16

**Date reviewed:** 2013-09-28 21:03

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<input type="checkbox"/> High priority for publication
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		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

The study is well designed and describe a new murine model of colitis caused by the administration of 1.5% DSS with a high interest for the evaluation of treatments for ulcerative colitis with mild to moderate activity . Mayor comments. At the end of the discussion should be added a paragraph of conclusions that reflect a more comprehensive conclusion of the abstract: DSS 1,5% for 9 days induced a mild colitis in which dysbiosis showed a pivotal role during the acute phase but chronic colitis occurred despite dysbiosis subsided.