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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 31616
Title: Disruption of the TWEAK/Fn14 pathway prevents 5-fluorouracil-induced diarrhea in mice.
Reviewer's code: 03262698
Reviewer's country: Italy
Science editor: Yuan Qi
Date sent for review: 2016-11-29 16:35
Date reviewed: 2016-12-23 15:30

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 work is interesting however I have some suggestions: 1. Introduction (line 6): please clarify and add reference to "prevent the development of drug resistance". 2. Results: in the section "Fn14 KO mice are resistant to the side effects of 5-FU" I suggest to remove the first sentence "Diarrhea is a critical indicator of chemotherapeutic agent-induced adverse effects in the intestine." 3. Results: Please check: figure 1 A, B and so on cited in the text do not correspond to the figure at the end of the file. 4. Results: There are some data not shown that should be added (also in the method section, i.e. apoptosis, proliferation and expression of transporter genes related to diarrhea). 5. Results: I suggest to add a subparagraph in the results on IL-13R?1 KO mice, making a separate figure for data of Figure 3B and C 6. Discussion: I suggest to move from "Fn14 is often upregulated in malignant tumors" (pag 19)… to … "Careful investigation of the effects of blocking TWEAK/Fn14 signaling on each cancer cell type is needed." (pag. 20) at the beginning of the discussion. 7. Discussion: I suggest to change the first sentence: "Blocking the TWEAK/Fn14 pathway suppressed 5-FU-induced diarrhea." In "Blocking the TWEAK/Fn14 pathway suppressed 5-FU-induced diarrhea, but did not

affect tumor growth in the CT26 tumor-bearing model or the antitumor effects of 5-FU." (from the sentence at pag. 19 "In our study, blocking the TWEAK/Fn14 pathway did not affect tumor growth in the CT26 tumor-bearing model or the antitumor effects of 5-FU."). 8. Discussion: I suggest to remove the sentence "Additionally, Fn14-deficiency could result in lower levels of other inflammatory cytokines, such as TNF-α, IFN-γ, and IL-17A, which also might affect IL-33 cleavage by inflammatory cells. Further studies are needed to investigate IL-33 processing, cellular localization, and function." 9. Figure legends/statistics: different tests have been applied (Two-way ANOVA with Bonferroni correction, one-way ANOVA, Students t test, Mann Whitney test), this choice must be justified and significance of each time versus day 0 within single group and of KOmice versus WT within single time must be showed.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 31616
Title: Disruption of the TWEAK/Fn14 pathway prevents 5-fluorouracil-induced diarrhea in mice.
Reviewer's code: 03262112
Reviewer's country: Italy
Science editor: Yuan Qi
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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

Peer review on manuscript n. 02461126 Disruption of the TWEAK/Fn14 pathway prevents 5-fluorouracil-induced diarrhea in mice This article concerns with a complete, innovative, very well defined and structured molecular study with important consequences on common clinical oncological practise. A molecular strategy is elaborated to prevent common 5FU adverse effect like anorexia and diarrhoea, symptoms that can reduce patient's compliance to chemotherapy. The manuscript presentation is clear, readability is very good, very good English level. Author contribution, Grant support, animal care are well defined in the title page. The title reflects the major topic and content of the study; it is focused and synthetic. The Abstract is well structured and clearly defines the study, respecting the sections and with a clear synthesis. The manuscript defines every detail of the study: the reader is provided of all information to completely understand the matter even if surgeon (like me!). Every section is really appropriated into its matters: intrioduction, materails and methods well describe in detail the experimetal study. Pathology is well descripted with attention to the topic. Discussions give complete argumentation on the basis of literature in

terms of recent researches: the analysis of literature is complete and exhaustive. Figures are original, reflecting an original and well structured study; they are well explained into legends. The references are appropriate, relevant and up to date. In my opinion the manuscript should be accepted. Great best regards and thank You all for the confidence.