

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 21199

Title: Association of Fusobacterium nucleatum with immunity and molecular alterations in colorectal cancer

Reviewer's code: 00928913

Reviewer's country: Taiwan

Science editor: Ya-Juan Ma

Date sent for review: 2015-07-04 18:59

Date reviewed: 2015-07-25 11:36

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

Nosho K et al. presented a review article regarding the association between the gut microbiome, immunity and molecular alterations in colorectal cancer (CRC) patients for a better understanding of the relationship between microorganisms and immune cells in the tumor microenvironment. They showed that the frequency of F. nucleatum positivity in the Japanese colorectal cancer was 8.8% (44/511), which was lower than that in U.S. cohort studies (13%, 76/598). Similar to the U.S. studies, F. nucleatum positivity in Japanese colorectal cancers was significantly associated with microsatellite instability (MSI)-high status. This finding indicates that molecular features of CRC, especially MSI, influence T-cell-mediated adaptive immunity, and F. nucleatum possesses immunosuppressive activities by inhibiting human T-cell responses. MicroRNA-21 increases the levels of IL-10 and prostaglandin E2 (PGE2), which suppress antitumor T-cell-mediated adaptive immunity through the inhibition of the antigen-presenting capacities of dendritic cells and T-cell proliferation in CRC cells. The review seems informative and appealing; however, there are a lot of criticisms and have several issues that the authors need to address before the manuscript is suitable for publication.

Major Compulsory Revisions:

1. The major concern of the current study is the frequency of *F. nucleatum* positivity in the Japanese colorectal cancer was 8.8% (44/511), which was lower than that in U.S. cohort studies (13%, 76/598). If authors would say it on the more solid evidence, they should compare both cohorts by the statistical analysis.
2. Authors mentioned in the text that microRNA-31 (miR-31) expression is significantly up-regulated in BRAF-mutated cancers compared with that in wild-type cancers using microRNA array analysis. In the current study, *F. nucleatum* positivity is also closely associated with BRAF-mutated cancers (Table 1). If any connection exists between miR-31 and *F. nucleatum*, and any relevant information is present regarding immunity and miR-31 in CRC tumorigenesis?
3. In most studies, MSI in colon cancer has been associated with improved survival. We are curious about if MSI status in Japanese CRC patients would be related to survival.

Minor Essential Revisions:

1. Figure 1 should be a hypothesis of potential mechanism and this must be present in the text.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 21199

Title: Association of Fusobacterium nucleatum with immunity and molecular alterations in colorectal cancer

Reviewer's code: 02397907

Reviewer's country: Czech Republic

Science editor: Ya-Juan Ma

Date sent for review: 2015-07-04 18:59

Date reviewed: 2015-08-12 00:07

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The manuscript no.: 20150630083237 submitted by Nosho et al deals with timely and highly relevant topic. Connection between human intestinal microbiome, host immune response, and microRNA regulation is now very attractive for eventual targeted therapies. Manuscript is written in comprehensive way and will attract readers with both experimental and clinical background. It fits well the WJG scope. Article fulfills very high standard in terms of clarity, language, and scientific rigor. Minor comments: Page 8, line 9 from bottom: delete "on" Page 9, line 6 from top: ... a host immune response is ... missing word response

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 21199

Title: Association of Fusobacterium nucleatum with immunity and molecular alterations in colorectal cancer

Reviewer's code: 02478901

Reviewer's country: Sweden

Science editor: Ya-Juan Ma

Date sent for review: 2015-07-04 18:59

Date reviewed: 2015-07-30 15:41

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

I found your manuscript very interesting and well written, but it seems more like a chapter for a textbook.