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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 23600
Title: Dissecting Characteristics and Dynamics of Differentially Expressed Proteins during Multistage Carcinogenesis of Human Colorectal Cancer
Reviewer's code: 03321763
Reviewer's country: Germany
Science editor: Yuan Qi
Date sent for review: 2015-12-07 11:16
Date reviewed: 2015-12-18 15:42

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[Y] 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	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The manuscript "Dissecting Characteristics and Dynamics of Differentially Expressed Proteins during Multistage Carcinogenesis of Human Colorectal Cancer" by Fang Peng et al. elaborated the protein profiles during multistage colorectal carcinogenesis as a potential diagnostic, prognostic or therapeutic tool. They used iTRAQ 2D LC-MS/MS in combination with laser capture microdissection (LCM). They detected 36 differentially expressed proteins, where 4 DMBT1, 5100A9, Galectin-10 and S100A8 were also evaluated by immunohistology. DEPs were involved in multiple biological processes, some with progressive up and some with progressive downregulation. The study was performed with 5 normal colon, 8 adenoma, 5 cancer in situ and 9 invasive cancer samples, where tissue samples were pooled after LCM selection. In 2 iTRAQ experiments they qualified 3123 proteins with 0% false positives. The authors then defined 379 proteins as shared, which were used to determine the experimental variations and the threshold for fold-changes. They then defined the number of proteins differentially expressed between NC, AP, CIS and ICC. A GO enrichment revealed upregulation of genes involved in expression and downregulation of genes involved in

energy and metabolic processes. Proteins upregulated in CIS were cell-cycle and adhesion related. ICC mostly showed upregulation of proteins involved in complement activation, fatty acid oxidation and coenzyme metabolic processes. The authors proceeded with a cluster analysis. Finally, the authors checked by imunohistology the 4 top ranked proteins in independent tissue samples. They adequately discuss results, where the limitations of our current state of knowledge become obvious. Taken together, although the manuscript remains at the descriptive level, the proteomic approach to compare different stages in colorectal carcinogenesis is very much appreciated. I need to say that I am not an expert in statistics. Thus, I cannot judge on this point. Nonetheless, for my understanding, statistics were well done. I have no major concerns. I would appreciate some more references in the discussion. And I suggest to put data in suppl. Table 1 into a database, as very few readers actually will be interested in the raw data, which they can look up from a deposit.

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
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[Y] Grade B: Very good	[Y] 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
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[ ] Grade E: Poor		[Y] No	[ ] Major revision
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		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This paper provides practical and novel proteomic information that is currently not known with respect to the expression of various proteins during colon carcinogenesis. Overall, the data presented was interesting, and with reorganizational editing of the paper and reworking the data to improve the understanding of the findings, I believe that it will be a good publication that would be very informative. The following are my specific comments about the manuscript in approximate order: 1. A better explanation of the iTRAQ technique in the introduction would help the reader understand how the technique provide quantitative information. This is a critical point about the technique vs other mass spectrometry approaches. 2. Figure 1 and 2 in the paper should probably be moved to the supplemental figures and the description should be moved to the methods. It is sufficient to discuss the results of the two repeat experiments in the methods as it is not experimental data per se. 3. Figure 1 should really be the Venn diagrams of comparisons of the different proteins from the different stages. It would be informative to have all the permutations of the comparisons between the different stages presented (i.e. NC vs AP, NC vs CIS, NC vs ICC, etc.) as Venn diagrams

which is originally what I thought that Figure 1 was. 4. I think that the paper could benefit highly from presenting a table of the top 5-10 different proteins between the different stages. Though this information could be obtained from the supplemental, it would be great to have the top candidates highlighted in the main paper. 5. Figure 3 should label the Y axis even though they are percentages it is not clear to the reader what percentages they represent. 6. Figure 4 has very poor resolution and no axis labels. 7. There needs to be a better explanation of the clustering and grouping from the reactome analysis. Figure 5 has little in the way of explanation, what is being compared? How are the items clustered? What does this tell us about the proteins expressed at the different stages? 8. Figure 6 also should have the rows/columns of pictures labeled. 9. The first paragraph of the discussion (as well as the remaining discussion) is difficult to understand and would benefit greatly from separating in the explanations into different paragraphs. The discussion should be reorganized to address a) the limitations of the techniques, b) the top most significant findings and c) what does their data say in the context of what is known. 10. Otherwise, there are small grammatical errors throughout the manuscript and the overall paper would benefit greatly from a careful edit.

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ESPS PEER-REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[Y] Accept
[Y] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
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COMMENTS TO AUTHORS

I have uploaded my comments in the word attachment.Please respond to my comments. Best wishes Mr Uppara