



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 46020

**Title:** NMR-based metabolomics and metabolic pathway networks from patient-matched esophageal carcinoma, adjacent noncancerous tissues and urine

**Reviewer's code:** 00182114

**Reviewer's country:** Japan

**Science editor:** Ruo-Yu Ma

**Reviewer accepted review:** 2019-01-25 10:42

**Reviewer performed review:** 2019-01-26 01:43

**Review time:** 15 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Apart from genomic and proteomic alterations, EC development and progression are associated with cellular metabolic changes that may provide insight into disease pathogenesis. 1H-NMR-based metabolomic findings identified distinct disturbances to



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EC patient urine metabolites, compared with HCs, including elevated acetoacetate, glutamate, cis-aconitate, citrate and reduced creatinine,, glycine, hippurate, ,taurine glucose. Altered urine metabolite levels could indicate perturbed amino acid metabolism, glycolysis, TCA cycle, urea cycle, choline metabolism, and gut microflora metabolism. I ask some questions to author. 1. Please tell me the reason why EC patient urine metabolites, compared with HCs, including elevated acetoacetate, glutamate, cis-aconitate, citrate and reduced creatinine,, glycine, hippurate, ,taurine glucose. 2. Which is the most sensitive predictor of esophageal cancer in urine metabolite? 3. Please tell me the different metabolomic profile between stage1,2 EC and stage 3,4 4. According to author's data, amino acid in tissue level is specific parameter, high level of valine, leucine,glutamate, acetate, alanine,choline, succinate , citrate and low level of glucose,creatinine,glycine, threonine, creatine, glutamine, taurine. How about serum level of amino acid in EC patient? Is the tissue level of amino acid in EC patients same pattern of serum level of amino acid in EC patient?

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- The same title
- Duplicate publication
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[ Y ] No



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 46020

**Title:** NMR-based metabolomics and metabolic pathway networks from patient-matched esophageal carcinoma, adjacent noncancerous tissues and urine

**Reviewer’s code:** 02941461

**Reviewer’s country:** Netherlands

**Science editor:** Ruo-Yu Ma

**Reviewer accepted review:** 2019-02-18 07:48

**Reviewer performed review:** 2019-02-20 18:37

**Review time:** 2 Days and 10 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer’s expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Hereby I would like to comment on the article entitled: “NMR-based metabolomics and metabolic pathway networks from patient-matched esophageal carcinoma, adjacent noncancerous tissues and urine” by the authors JIA-Hao Liang. The authors show



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potential metabolic changes in esophageal cancer tissue and according changes in metabolic signature in urine samples. Although these are interesting and potentially important findings, I also have some concerns. Major

1. The authors identify certain metabolites to be changed in esophageal cancer tissue compared with healthy tissue and this is validated only in 16 patients (8 EC and 8 HC). I think this group is too small for validation and this strongly limits the conclusions from this exploratory research.
2. Stage of the tumour may be an important factor in the changes observed, especially in stage IV disease. In the 17/41 patients, the tumour stage was not unknown. This should be further specified or at least an attempt should be made to have limit these missing data.
3. Figure 1 is not clear to me. This may be further clarified by indicating the important parts of this figure, or can be omitted and explained in the text to improve readability

Other points

1. In the abstract it is stated that colonic tissue was used, I think the authors mean esophageal tissue
2. The Variable Importance (VIP) needs more extensive explanation in the discussion
3. The results section of the abstract must be more specific
4. The discussion can be compacted substantially.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- The same title
- Duplicate publication
- Plagiarism
- No

##### ***BPG Search:***

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[ Y ] No