

6 February 2014

Dear Dr Wang:

Please find enclosed the edited manuscript in Word format (*ESPS Manuscript No 6787-review*)

Title: The potential role of metabolomics in diagnosis and surveillance of gastric cancer

Authors: Angela W. Chan, Richdeep Gill, Daniel Schiller, Michael B. Sawyer

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript No: 6787

The manuscript has been improved according to the suggestions of reviewers. All changes are highlighted in red.

Reviewer#1 (Major Revision)

Altogether, this is an interesting well structured review for an evolving topic. Nevertheless, there are more studies referring to the metabolomics in diagnosis and surveillance of gastric cancer. I would expect a more comprehensive report of these studies. The recent report of Abbashi-Ghadi et al. EJC 2013 describes analytically the role of metabolomics in gastric cancer. In order your report to add something new in the literature the critical appraisal of all the studies referring to your topic will be required. Minor comments: The second paragraph in the amino acid metabolism deals with squalene. I think this should be under the "Fatty acid metabolism". It would be interesting to comment more on the other methods used for metabolomic assessment, especially concerning the accuracy of these methods.

Response to Reviewer #1

- More studies have been added to provide a more comprehensive review
- The recent report by Abbashi-Ghadi et al was already included on the original manuscript from October 2013; however, more information from that systematic review has been added
- The discussion section provides a critical appraisal of studies, including weaknesses in the study designs, research methodology flaws, and reasons for metabolite inconsistencies.
- The squalene comments are now moved under "Fatty acid metabolism"
- The methods for metabolomic assessment (liquid/gas chromatography, NMR, and mass spectrometry) have been explained, with a comparison of the sensitivity of each analytical platform

Reviewer#2 (Rejection)

This is a potentially interesting review manuscript as it could provide evidence into current research practice in gastric cancer. However, now, the manuscript is still not clearly presented. The manuscript should be extensively improved because the manuscript titled 'The potential role of metabolomics in diagnosis and surveillance of

gastric cancer'. This article is going to give a brief overview of metabolomic investigation of gastric cancer. However, without discussion section, the authors did not offer their own perspectives. Furthermore, tables and figures may be the most effective way to communicate the findings in the review. I suggest authors can make resubmission if the above points are addressed and substantial improvements are made.

Response to Reviewer 2:

- A discussion section has been added where we offer author perspectives and critiques of previous studies
- Two new tables have been added. Table 1 is a summary of studies comparing statistically different metabolites between normal and cancer subjects. Table 2 compares metabolites across cancer stages.

Reviewer#3 (Minor Revision)

- 1-Thank you for your review. This field is open for new studies in future.
- 2-"Core Tip" can be more highlighter
- 3-Conclusion could be developed.
- 4-Could you please explain; we can look at what methods? (under "Metabolomics in Cancer")

Response to Reviewer 3:

- The core tip has been revised to be more comprehensive.
- The conclusion has been developed to be more comprehensive. We mention the research that our lab group is performing to add to the current body of literature on gastric cancer metabolomics
- Under "Metabolomics in Cancer" method, the chromatography and mass spectrometry methods are further explained.

There has been a mutual agreement amongst our group to switch the senior author. It is now Dr. Michael Sawyer rather than Dr. Daniel Schiller.

Thank you for considering our manuscript for publication in the *World Journal of Gastroenterology*.

Yours truly,



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