

March 24<sup>th</sup>, 2014

Dear Editor,

Please find the attached manuscript in word format (file name : 8511-review)

**ESPS Manuscript** NO: 8511

**Title:** Biomarkers of barrett's esophagus

**Author Name:** YM Fouad, Ibrahim Mostafa, R Yehia and H R El-Khayat

**Name of Journal:** *World Journal of Hepatology*

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewers

4 We thank all reviewers who accepted our review

Please find below the reply to reviewers.

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Best regards

Sincerely

Dr Yasser M Fouad MD Do

Professor of Gastroenterology and Hepatology

Reviewer #1

1- The core tip and author contribution is repeated

Reply: corrected in revision

2- Abbreviations need to be explained

Reply: corrected in revision (highlighted)

3- Esophagus not eosophagus:

Reply: corrected

4- Definition of BE metaplasia is disputed and this should be alluded

Reply: added paragraph (highlighted)

5- Second paragraph in the introduction is unnecessary :

Reply: eliminated and reference 6 was added to previous references.

6- 3<sup>rd</sup> paragraph is misleading and figure 1 in appropriate:

Paragraph was revised and figure was eliminated

7-Definition:

Identification not production

Reply: corrected

7- Types not mechanisms of biomarkers :

Reply : corrected (highlighted)

8- C- hyper methylation of should be discussed under epigenetics:

Corrected (highlighted)

9- Classification of biomarkers should be highlighted and table 1 quoted :

Reply: done

10- Biomarkers in clinical field and summary should be rewritten:

Done

Reviewer # 2

1) The biomarkers presented here include two types 1) ones postulated to be useful in patients with BE (for example, predicting risk of progression), and 2) ones which may predict prognosis or response to therapy in patients with esophageal adenocarcinoma. Although the authors make some effort to divide the biomarkers by class, it is difficult to understand the utility of a particular biomarker since these two conditions are mixed together. For many biomarkers, data on clinicopathologic significance is more firmly established for one condition (e.g., esophageal adenocarcinoma) I suggest dividing the review of specific biomarkers more explicitly into separate sections covering BE and esophageal adenocarcinoma (both in the text and in the table). Some biomarkers may be cited in both sections.

Reply:

Thank you for this valuable comment. The authors believe that the overlap in the biomarkers make this suggestion difficult to perform

2) Phases of biomarker production: p.5 bottom- This section would be more accurately described as biomarker validation

Reply: corrected

3) p.6- LOH conventionally stands for loss of heterozygosity, and I believe that is the meaning here.

Reply : corrected

4) p.7, section d, first sentence - This sentence should begin as "Epigenetics refers..."

Reply : corrected

5) p.7 last line- Insert the word "Cyclin D1 <overexpression> has been shown to be."

Reply: inserted

6) p. 8- I would view Ki67 as a nonspecific marker for dysplasia

Reply: I agree with you.

7) p.9-11 classification of biomarkers – I would place this section before consideration of individual biomarkers. Then, literature review can be placed in better context.

Reply: good suggestion. corrected

8) In the conclusion, the authors should offer an opinion on the most promising biomarkers for management of patients with Barrett's esophagus and esophageal adenocarcinoma.

Reply: the conclusion was rewritten according to suggestion of both review