

October 26, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5740-review.doc).



Title: Advance of epigenetic biomarker study in colorectal cancer

Author: Xi Wang, Yeye Kuang, Xiaotong Hu

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5740

The manuscript has been improved according to the suggestions of reviewers: Format has been updated. And the revision has been made according to the suggestions of the reviewers.

Comment 1:

The paper is disseminated of typing errors (i.e.: Introduction: not fetal-occult but fecal-occult) and grammar faults. Please perform a thorough revision of the language.

Answer:

The paper has been edited by the English language editing companies American Journal Experts.

Comment 2:

In this paper, a comprehensive overview of progress in epigenetics research and the biomarker studies in colorectal cancer was summarized. It would be better to make a little of revision and language polishing for publication.

Answer:

The paper has been edited by the English language editing companies American Journal Experts.

Comment 3:


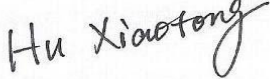
The present review on epigenetic biomarkers for potential use in handling and treatment of patients with colorectal cancer is timely, well-written and has a lot of prominent issues in focus. In addition, that specific issue is "hot" at present. Everybody (almost) is looking into epigenomic phenomena – with the risk that much improper results are presented. Therefore, the present review gives information on where the discipline has reached.

There are however some discrepancies that must be corrected before publication can be recommended.

1. Inflammatory bowel diseases are not precursors for CRC. It's only a risk factors in line with other diseases such as diabetes.

2. At the time of primary diagnosis 80% of the patients are offered resection and potentially are cured by that. However, 40-45% of these patients experience a later recurrence and was therefore not cured by resection. However, it's not correct to write that only 30-40% of the patients have resectable disease.
3. Only colonoscopy is the gold standard for early detection. And certainly FOBt is only a risk finding tool. Those with occult stool blood must be offered subsequent colonoscopy.
4. The sentence "*postoperative tissue sampling may be more effective for prognosis, including the prediction of mean survival, resectability of the primary tumor and the administration of targeted therapies*" is without any understandable information. It must be corrected.
5. Re. the methylation paragraph: xenograph tumors do not give informations on prognostics biomarkers when the focus is reaction to therapy – it is prediction biomarkers.
6. On page 7: persons with lack of sept9 methylation expression are not "patients"
7. On the very same page: you can't deal with a mix of stool and plasma biomarkers – just "handle" them separately and then discuss pros and cons for the various approaches.
8. On page 8/9 the authors must include a short comment of the very limited compliance when using fecal biomarkers – often less than 50%. Therefore, the biomarkers are not the only thing to address.
9. Re. all the minor studies that the authors refer to – have they ensured that these studies are done according to requirements of the REMARK guidelines. By that it's ensured that the various samples are collected in the very same manner at the very same time. It's completely out of proper science to use for instance newly collected samples from CRC patients and compare results of such sampling analyses with archived samples from adenoma patients or healthy persons. By doing so the bias is enormous and results not interpretable.

are reviewer's comments in this revised version

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