

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 12026

Title: Hyperhomocysteinemia as a potential contributor of colorectal cancer development in inflammatory bowel diseases: A review

Reviewer code: 00068723

Science editor: Yuan Qi

Date sent for review: 2014-06-18 16:44

Date reviewed: 2014-07-05 15:46

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|---|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A: Excellent | <input checked="" type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> Existing | <input type="checkbox"/> High priority for publication |
| <input checked="" type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade D: Rejected | BPG Search: | <input checked="" type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | <input type="checkbox"/> Existing | <input type="checkbox"/> Major revision |
| | | <input type="checkbox"/> No records | |

COMMENTS TO AUTHORS

This review is a rare theme on hyperhomocysteinemia and carcinogenesis. "4. Homocysteine metabolism and pathogenesis of hyperhomocysteinemia" illustrates background information synergistic with Figure 1. Interesting point is a potential application of hyperhomocysteinemia as a tumor marker of colorectal cancer. The relation between hyperhomocysteinemia and colorectal cancer was not clear. Does hyperhomocysteinemia promote carcinogenesis of colorectal cancer? Are there any experimental evidence on this? How do serum levels of homocysteinemia change during progression from IBD to colorectal cancer? Do the authors have any speculation on role of hyperhomocysteinemia in carcinogenesis of colorectal cancer?

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Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 12026

Title: Hyperhomocysteinemia as a potential contributor of colorectal cancer development in inflammatory bowel diseases: A review

Reviewer code: 00068278

Science editor: Yuan Qi

Date sent for review: 2014-06-18 16:44

Date reviewed: 2014-07-09 20:51

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|--|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A: Excellent | <input checked="" type="checkbox"/> Grade A: Priority publishing | Google Search: | <input checked="" type="checkbox"/> Accept |
| <input checked="" type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> Existing | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade D: Rejected | BPG Search: | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | <input type="checkbox"/> Existing | <input type="checkbox"/> Major revision |
| | | <input type="checkbox"/> No records | |

COMMENTS TO AUTHORS

This is a well written review. As already stated, the relation between hyperhomocysteinemia-folate deficiency and colorectal cancer is still open to question. A minor correction: Page 9, line 8, must be .. dysplasia-associated lesions or masses, or colorectal CARC?NOMA in 114 IBD patients.

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 12026

Title: Hyperhomocysteinemia as a potential contributor of colorectal cancer development in inflammatory bowel diseases: A review

Reviewer code: 02438768

Science editor: Yuan Qi

Date sent for review: 2014-06-18 16:44

Date reviewed: 2014-07-12 22:40

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|---|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A: Excellent | <input checked="" type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> Existing | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> No records | <input checked="" type="checkbox"/> Rejection |
| <input checked="" type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade D: Rejected | BPG Search: | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | <input type="checkbox"/> Existing | <input type="checkbox"/> Major revision |
| | | <input type="checkbox"/> No records | |

COMMENTS TO AUTHORS

Comments for ESPS Manuscript NO: 12026 Hyperhomocysteinemia is associated with inflammation and may be a risk marker for colorectal cancer. However, so far, it is not clear if hyperhomocysteinemia is associated with increased colorectal cancer risk in IBD patients, as stated by the authors themselves in Conclusion. In addition, plasma total homocysteine levels significantly increased in a variety of tumor patients, however, homocysteine levels in the body can be affected by a number of factors. Should it be adopted as a tumor marker, its low specificity would mean a very limited clinical application. I have some comments regarding the manuscript. 1.No critical supportive data are intended for demonstrating that hyperhomocysteinemia can promote colorectal carcinogenesis. 2.There is little evidence for a mechanistic relation between hyperhomocysteinemia and increased risk of colorectal cancer in IBD patients, though the authors claimed that they would review the mechanisms between them. In short, in my opinion, although this review bears an important topic, its content carries little scientific and clinical importance in its current form.

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 12026

Title: Hyperhomocysteinemia as a potential contributor of colorectal cancer development in inflammatory bowel diseases: A review

Reviewer code: 01441415

Science editor: Yuan Qi

Date sent for review: 2014-06-18 16:44

Date reviewed: 2014-09-09 16:57

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|--|--|-------------------------------------|---|
| <input type="checkbox"/> Grade A: Excellent | <input checked="" type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input checked="" type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> Existing | <input checked="" type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D: Fair | | BPG Search: | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | <input type="checkbox"/> Grade D: Rejected | <input type="checkbox"/> Existing | <input type="checkbox"/> Major revision |
| | | <input type="checkbox"/> No records | |

COMMENTS TO AUTHORS

This review manuscript by Keshteli et al. summarized current knowledge regarding the role of hyperhomocysteinemia and colorectal cancer in IBD patients in a comprehensive fashion. Although, the evidence for the direct mechanism for cancer development is sparse, the topic itself is quite attractive and promising. The authors mentioned about MTHFR C677T polymorphisms in this manuscript. This polymorphism seems to predominantly contribute to hyperhomocysteinemia. It is also known that the polymorphism is functional, relatively common mutation (the T allele frequency is reported to be 0.33). Reported genetic studies suggested the association between the polymorphism and cardiovascular diseases. If studies investigating the association between the polymorphism and colon cancer (and/or IBD) exist, please mention it.