

December 24, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 7576-review.doc).

Title: Mechanisms linking dietary fiber, gut microbiota and colon cancer prevention

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Name of Journal: *World Journal of Gastrointestinal Oncology*

ESPS Manuscript NO: 7576

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 reviewer

(1) **Reviewed by 00068485:** This is a very interesting review covering some important cellular effects of short chain fatty acids. Some points to consider: 1. page 5 line 19 - uncertain what is meant here 2. In section 6 on the role of SCFA on cell kinetics - it would be useful for the authors to conclude their thoughts if changes in butyrate content with the colonic lumen and its effects are sustained and if so for how long? 3. Pg 13 - section 7. It's not clear if the authors propose that phytochemicals/SCFA themselves or gut microbiota act as signalling molecules in colon cancer? 4. In Figure 1 - should there not be a question mark also for the pathway effects of dietary fibre and net effect on adenoma formation - it's not firmly established yet.

Response: 1) This is a summary sentence, and we reworded and included more references to help readers (page 4, line 31-33); 2) The role of SCFA on cell kinetics depends on the composition of SCFA and cell types, and we are not able to generalize the timing. However, in this section, we did provide a broader picture of a multifaceted role of SCFA production/action; 3) Yes, they are phytochemicals. We also reworded the sentence and deleted "by functioning as signaling molecules" because it appears to be too specific (page 11, line 24-26); 4) Revised the Figure and its legend.

(2) **Reviewed by 02551508:** No comments.

(3) **Reviewed by 01587889:** This fine article put together many epidemiological and experimental studies that have suggested that dietary fiber plays an important role in colon cancer prevention. These findings may relate to the ability of fiber to reduce the contact time of carcinogens within the intestinal lumen and to promote healthy gut microbiota, which modifies the host's metabolism in various ways. Elucidation of the mechanisms by which dietary fiber-dependent changes in gut microbiota enhance bile acid deconjugation, produce short chain fatty acids, and modulate inflammatory bioactive substances can lead to a better understanding of the beneficial role of dietary fiber. This article reviews the current knowledge concerning the mechanisms via which dietary fiber protects against colon cancer. Good work indeed. However I have few suggestions that could improve quality of this paper as follows: In introduction: Page 2 Line 25 - I don't see diet or

physical activity being an environmental exposure – perhaps an example be environmental toxicants. Are the authors inferring that diet is contaminated via environmental exposure? This is unclear. Impact of dietary fiber on gut microbiota: Page 4 Line 1-14 – I think it would be helpful to briefly explain how changes in bacterium production is helpful and/ or detrimental i.e. state that butyrate is harmful to colon cancer cells and that increased sulphate- reducing bacteria are linked to colon tumors.

Response: 1) The definition of “environment” is based on National Institutes of Health (USA) (<http://www.cancer.gov/cancertopics/understandingcancer/environment/AllPages>):

When most people think of the word "environment," they think of forests, oceans, or mountains. In cancer research, however, scientists define the environment as everything outside the body that enters and interacts with it. This interaction is called an exposure. So, environmental exposures can include such factors as sunshine, radiation, hormones, viruses, bacteria, and chemicals in the air, water, food, and workplace, as well as lifestyle choices like cigarette smoking, excessive alcohol consumption (more than 2 drinks/day), an unhealthful diet, lack of exercise, or sexual behavior that increases one's exposure; 2) Impact of dietary fiber on gut microbiota and its functional consequences have been discussed on Page 4, line 10 to 33.

3 References and typesetting were corrected

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

Sincerely yours,



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