

September 12, 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name:adaptation—09-11.doc).

Title: Intestinal mucosal atrophy and adaptation

Author: Darcy Shaw, Kartik Gohil, Marc D. Basson

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 156

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

1 Format has been updated and verified.

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

The reviewer suggested that we add a mention of the question of why small bowel cancers are much less common than colon cancers in humans and why APC/MIN mice more commonly get small bowel neoplasms to our table of unanswered questions. We have done so, and we have also added a new paragraph of text that relates to this issue.

Our text now contains the following paragraph (pages 8-9)

The anatomic location of the bowel mucosa has an important relationship with adaptive biology. The small and large intestinal mucosa demonstrate many differences in histology, cell phenotype, and transport proteins that reflect their differences in normal function. In addition, the small and large intestinal mucosa respond differently to stimuli of malignant transformation. For example the APC(Min) mouse is a dominant mutation that leads to multiple intestinal neoplasia.^[97] Crypt cells express a balance of proliferation and differentiation, a process with aberrant regulation in these mutants. In mouse models with this mutation, small bowel neoplasms are much more common than colonic neoplasms, in contrast to the human condition in which colonic neoplasms are more common.^[98] The reason for this regional difference is as yet unknown but further investigation may offer important clues into differentiated intestinal epithelial biology.

In addition, the table 4, "Question for future study" now contains the following additional questions:

Why is neoplasm more common in the large intestine than in the small intestine?

Why is neoplasm more common in the large intestine than in the small intestine?

Why do APC(Min) mice have more common neoplasms in the small bowel?

Each of these has been also highlighted in the text of the final manuscript for the reviewer's convenience as indicated here.

3 References and typesetting were corrected

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

Sincerely yours,

Marc D. Basson, MD, PhD