

Format for ANSWERING REVIEWERS



March 24th 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 9622-review.doc).

Title: ULCERATIVE COLITIS: FROM INFLAMMATION TO CANCER. IS THERE A ROLE FOR ESTROGEN RECEPTORS?

Author: Mariabeatrice Principi, Michele Barone, Maria Pricci, Nicola De Tullio, Giuseppe Losurdo, Enzo Ierardi, Alfredo Di Leo

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 9622

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

Reviewer 1

It is an interesting and well-written review regarding estrogen receptor in UC-CRC. I only have a few comments.

- 1) The 1st sentence of the 2nd paragraph in "Ulcerative colitis, from inflammation to cancer", do you mean incidence of CRC in UC patients or incidence of UC? It is unclear to me.
As clarified in revised manuscript, we report the incidence of CRC in UC.
- 2) Some editing needs to be done in the last paragraph of "Estrogen receptor expression in the progressive stage of ulcerative colitis related carcinogenesis". The authors stated that Ki-67 expression revealed a more marked significant raise, you meant in UC-low-grade dysplasia? It is unclear to me. In addition, there is an incomplete sentence in the paragraph.
In revised manuscript, we clearly reported that Ki-67 showed a more marked increase than TUNEL in UC and LGD. However, all the paragraph was re-written in order to improve its comprehension.
- 3) The second half of the second last paragraph in "Future perspectives of chemoprevention by beta receptor agonists" needs to be rephrased. Ki67 expression increased after phytoestrogen administration? What is "labeling index"? In addition, the last paragraph has an incomplete sentence.
The paragraph has been re-phrased. Obviously, TUNEL/Ki 67 ratio was increased by phytoestrogen administration. Labeling index was clearly defined as the percentage of positive cells at immunohistochemistry.
- 4) Figure 2 is unclear to me.
Figure legend was completely re-written in order to obtain a full description of the figure for its comprehension.

Reviewer 2

The authors show the possibility of estrogens having effect on colorectal cancer development in

patients with UC. The review is well written and very interesting. I think no problems except only several missing ex. "mixed written colorectal and colo-rectal" in the manuscript.

A linguistic revision was performed by a native speaker.

3 References and typesetting were corrected

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

Sincerely yours,

Prof. Enzo Ierardi