

## ANSWERING REVIEWERS

January 3, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: ESPS Manuscript 7502-revised.doc).

**Title:** Xenoestrogens challenge 17 $\beta$ -estradiol protective effects in colon cancer

**Author:** Maria Marino

**Name of Journal:** *World Journal of Gastrointestinal Oncology*

**ESPS Manuscript NO:** 7502

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) It is a good review which will be useful to young investigators and to students. Only reservation is that a better sentence may be used for the title of this manuscript "...against colon cancer proliferation" is an inaccurate statement.

ACTION - I thank the reviewer for its comments. The title has been changed; it now is: 'Xenoestrogens challenge 17 $\beta$ -estradiol protective effects in colon cancer'

(2) This is a very nice review about the role and action mechanisms of E2 in colorectal cancer. The ability of xenoestrogens in the impairment of the E2 actions is also explored. The manuscript is very easy to follow and well written and deserves to be published in the World Journal of Gastrointestinal Oncology (WJGO). I do not have any concern about the content of this review. I just suggest do not use the acronym E2 in the titles of the sections and use the complete name 17 $\beta$ -estradiol.

ACTION - I thank the reviewer for these benevolent and encouraging comments. The acronym E2 has been removed from all section titles.

(3) Major comment

1. In the Introduction, it would be better that the contents about estrogen receptors is described next contents, "Effect of E2 in colon". To help understanding about the effect of E2, it needs more information about the action mechanism of each estrogen receptor. Also, if author add the figure about the action mechanism of each estrogen receptor, it would help understanding.

ACTION - Since many years our research group is working on dissecting the mechanisms of estrogen receptors, in these years we published several reviews on estrogen receptor action mechanism (see references 1,5,18,53,59,65) in which several figures and cartoons have been used to explain the action mechanism of these receptors. In this review the focus is on



estrogen and colon avoiding repetition with other review that have been cited and are easily achievable if the reader needs an in-depth analysis.

2. In the contents "3. Effect of E2 in colorectal cancer", the first paragraph is unnecessary. The second paragraph is suitable for introduction.

ACTION - The first paragraph has been extensively shortened, whereas the second one, after reduction, has been maintained as the indispensable introduction of paragraph "3. Effect of E2 in colorectal cancer",

3. Why did you separate the contents of "3. Effect of E2 in colorectal cancer" and "4. E2 action mechanism in colorectal cancer"? I don't know what is different between "3" and "4". It is better to combine the two contents and to describe in detail and systematically.

ACTION - From a didactic point of view, I consider important to separate hormonal effects (a phenomena that is produced by a cause or agent) from hormone action mechanisms (the explanation of a phenomena). However, following the suggestion of the reviewer the E2 action mechanism has been inserted as a subparagraph of "3. Effect of E2 in colorectal cancer"

4. In the contents "5. Xenoestrogen effect in colorectal cancer" and "conclusion, your description about the effect of xenoestrogen on colorectal cancer is very confusing. If there are more research about the effect of xenoestrogen on colorectal cancer, please add more information and describe clearly.

ACTION - I am sorry that this reviewer finds confusing this paragraph, but very scarce literature is present in the data bases on xenoestrogen and colorectal cancer. In fact, one of the goals of this review is to bring at the researcher attention the lack of literature concerning the effects of xenoestrogen on colorectal cancer hoping to stimulate more basic research on this issue.

Minor comment Please, correct as following. : Apc (Adenomatosis polyposis coli) ? APC (Adenomatous polyposis coli)

ACTION - The correction has been inserted.

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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