

Author's response to reviews

Title: The effect of body weight on altered expression of nuclear receptors and cyclooxygenase-2 in human colorectal cancers

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Version: 2 Date: 30 May 2007

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Talence, May 31, 2007

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to: Editorial Office
Nutrition Journal

Dear Editor,

On behalf of my co-authors, I am submitting a revised version of the manuscript entitled:

« The effect of body weight on altered expression of nuclear receptors and cyclooxygenase-2 in human colorectal cancers »

Being overweight increases the risk of dying from cancer. Specifically, being overweight is now recognized to increase the risk of developing colorectal cancer (CRC). However, little is known about the mechanisms mediating such association.

Therefore, the present report focused on the expression of key regulators of lipid metabolism involved in colorectal carcinogenesis. Alterations in the expression of nuclear receptors PPAR, RAR and RXR and of COX-2 have been investigated in patients undergoing surgery for CRC. The study also examined the hypothesis questioning the relationship between alterations in the expression of nuclear receptors and COX-2, and the weight status of the patients.

To our knowledge, this is the first time that such association has been investigated. We concluded that altered expression of these molecular targets was not associated with the weight status of subjects. We also found that COX-2 expression in healthy colon mucosa was affected by the body weight status of patients.

The entire manuscript was rewritten as strongly suggested by the reviewer's comments and we hope that it can now meet a favorable review. I look forward to your reply.

Sincerely,

Prof. P. Cassand

Reviewer 1:

Major compulsory revisions:

1] Abstract

The abstract was completely rewritten and the objective of the article is now clearly identifiable: answer the question of a possible association between the expression of nuclear receptors and COX-2, and the body weight status of patients undergoing surgery for CRC removal. Results concerning changes in COX-2 expression in colon mucosa were added in the result section of the abstract.

2] Background

The background has also been rewritten.

«Approximately 5% of individuals will develop colorectal carcinoma during their lifetime» **A reference was added: *Jemal A et al. Cancer statistics, 2004***

«Indeed, the etiology of CRC involves changes in cell environment and signal transduction related to dietary components» **The sentence was deleted.**

«COX-2 overexpressed in several epithelial cancers including CRC» **2 references were added: *Kutchera W et al. PNAS, 1996* and *Wolff H et al. Cancer Res 1998*.**

The reference *Marin HE et al. Cancer Res, 2006* (suggested by the reviewer) has been added in the background section to indicate that conflicting data have been described concerning the role of PPAR delta in colon carcinogenesis.

Fenofibrate activates PPAR alpha and antidiabetic pioglitazone activates PPAR gamma predominantly. **We only mentioned the drug family name thiazolidinedione (which includes pioglitazone).**

3] Results

The section has been slightly shortened since data concerning changes in PPAR gamma expression depending on the location (ascendant colon vs. other parts) were deleted (because it was difficult to interpret the results).

Table 3 now shows the association between nuclear receptor and COX-2 expression (data added).

4] Discussion

The discussion was rewritten and now focused on our results.

The entire manuscript was carefully edited.

Reviewer 2:

Major compulsory revisions:

As asked, the manuscript was carefully rewritten.

The abstract now mentions all the results.

Table 3 has been carefully filled.

Data concerning PPAR gamma expression in ascendant colon vs. other parts were deleted.

The sentence concerning PPAR delta and COX-2 co-localization was deleted because it was clearly confusing.