

Dear Editor,

We appreciate the work and efforts made by the Editors and Reviewers in reviewing our manuscript. We have corrected the manuscript following their comments and suggestions. References and Tables have been changed according to the Editor suggestions. Several sections have been now included to fulfill the requirements of the WJCO.

We believe that the revised manuscript has now been considerably strengthened. Please find attached the revised manuscript showing the highlighted changes: Yellow font: answers to Reviewers' comments and additional corrections.

Please find below our responses to the specific comments raised by the Reviewers.

Reviewers' comments:

Reviewer 1:

Minor language polishing

R:/ Language has been corrected in the revised MS.

Reviewer 2:

The authors wrote a comprehensive review on the topic of leptin and cancer, particularly on leptin signaling pathway involved in cancer development and chemoresistance.

1. This review covers a wide range of cancer type. Since this is a journal of gastroenterology, it is better to focus on the cancers of digestive system. The contents of other cancer types (e.g. breast cancer, thyroid cancer, lung cancer, prostate cancer.....) can be deleted from the ms.

R:/ We respectfully disagree with the Reviewer. The World Journal of Clinical Oncology publishes manuscripts dealing with a variety of malignant diseases, but not only those related to Gastroenterology. Therefore, we modestly consider that the issues discussed and presented in the manuscript are appropriated for readers of the WJCO.

2. The article "Leptin signaling enhances cell invasion and promotes the metastasis of human pancreatic cancer via increasing MMP-13 production" by Fan Y et al (Oncotarget, 20156:16120-

34.) is highly related to this review, and need to be cited in the review.

R:/ We agree with the Reviewer's comment. We have added the new reference. The main conclusions of the interesting paper published by Fan et al. were now included in the revised manuscript.

3. The structure of this ms is not clear. The subtitles and their corresponding contents need to be rearranged to have obvious hierarchy.

R:/ We agree with the Reviewer's comment. The revised manuscript has been changed according his suggestion. The introduction was shortened. A new section entitled: "Obesity, Leptin/OB-R and Cancer" now presents findings on these factors affecting cancer progression. Additionally, a new title for the sub-chapter dealing with leptin and Notch is now presented as "Leptin-induced Notch and RBP-Jk affect cancer progression". Similarly, the sub-chapters on leptin and breast cancer and cancer stem cells are now entitled "Leptin signaling induces breast cancer progression" and "Leptin signaling promotes the expansion of cancer stem cells". This last sub-chapter includes: "Breast cancer stem cells" and "Pancreatic cancer stem cells sub-sections".

Reviewer 3:

Interesting and really up-to-date review of clinically important topic.

R:/ We agree with the Reviewer.