

Dear Editor and Reviewers,

Thank you for your time in reviewing our manuscript titled, “Metabolic and inflammatory functions of cannabinoid receptor type 1 (CB1) are differentially modulated by Adiponectin”. Your insightful and constructive critiques have helped us to improve the manuscript greatly. We have carefully revised the manuscript to address all reviewers’ comments. Below please see our point-by-point responses (in bold text).

Sincerely,

Yuxiang Sun, Ph.D.

Reviewer #1:

The study is well designed and properly carried out. It reveals a new data regarding the cannabinoid receptors and their impact in adipogenesis, thermogenesis and insulin resistance. Minor remarks are to rephrase the sentence: These results suggest that rimonabant may regulates adiponectin expression in adipocytes, and that the metabolic effects of rimonabant could be due at least in part to due to enhanced adiponectin secretion, and to indicate several abbreviations:PBS, PGC etc

Reply: We appreciate the reviewer’s helpful comments and suggestions. We have revised the text as indicated below.

“These results suggest that rimonabant may regulate adiponectin expression in adipocytes, and the metabolic effects of rimonabant, at least in part, could be due to enhanced adiponectin secretion.”

Sorry about the oversight. We =have added full names of abbreviations for PBS, PGC1 and others.

Reviewer #2: I read your manuscript entitle “Metabolic and inflammatory functions of cannabinoid receptor type 1 (CB1) are differentially modulated by Adiponectin “interestingly. I have some minor point for increase the quality of paper 1. Please rewrite the abstract according to journal norm (250-300 words)

Reply: We appreciate the reviewer’s detailed comments and suggestions.

We have revised the abstract in WID journal format within 300 words.

2. Please define how evaluated the ITT and GTT variables (which device and which method), as well as add the necessary information such as detection range and intra and inter assay.

Reply: We have added text below in the material and method section:

“It can detect glucose concentrations from 20 to 600 mg/dl using an electrochemical biosensor technology based on glucose oxidase chemistry.”

3. Please give more reliable data about flow cytometry device and monoclonal antibody lot no.

Reply: We have added text below in the material and method section:

“Antibody information used is as follows: PE anti-mouse F4/80 antigen (eBioscience, San Diego, CA), FITC anti-mouse CD11c antigen (BD Bioscience, San Jose, CA), purified CD16/CD32 antigen (BD Bioscience, San Jose, CA), and APC anti-mouse CD206 antigen (BD Bioscience, San Jose, CA). All data were collected using a FACScan and analyzed using CellQuest software (BD Biosciences, San Jose, CA).”

4. Please define group study specifically, (where is control group)

Reply: We have added sentence below in the material and method and in figure legend. “There were three groups of mice: (WT) control group, CB1-/- group, and DKO group.”

5. Please complete the statically analysis (You did not use the non parametric tests)

Reply: We revised the sentence in data analysis.

6. Please add the primers use in this study.

Reply: According to the reviewer’s suggestion, we added primer list in table 1 in method section.

7. Please improve the header of table (The captions and descriptions of the tables are very vague)

Reply: There is no table in original main text, but we have tried to improve labels of all figures.

8. Please add the more new references in conclusion

Reply: We have replaced some references with more current ones.

Editorial office:

(2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Reply: We rearranged and edited all figures on PowerPoint file, and the PowerPoint file will be submitted in the revision.

(3) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text;

Reply: According to the editor's suggestion, we now have added article highlights at the end of the paper.

(4) Please download the The ARRIVE Guidelines at <https://www.wjgnet.com/bpg/GerInfo/287>, and fill it out with page numbers.

Reply: We have submitted approved animal protocol AN-2770 in the original submission.