

Lyon, January 23<sup>rd</sup>, 2017

Dear Editor,

Please find enclosed the revision of our manuscript **NO: 31581** (Invited minireview) entitled:

**“Role of pro- and anti-inflammatory phenomena in the physiopathology of type 2 diabetes and obesity”**

Which was submitted to the *World Journal of Biological Chemistry*

According to the reviewers and your requests, we are now submitting a revised manuscript that has addressed the editorial concerns and the suggestions of the reviewers.

We are very grateful to the editors and reviewers for their reviewing work, comments and helpful suggestions.

Beside this response letter we are submitting revised manuscript file and a newly added “Table 1”.

We believe that we have addressed all the comments in a satisfactory manner, and we hope that you and the reviewers will now consider our revised manuscript as acceptable for publication in *World Journal of Biological Chemistry*.

Sincerely yours, Luciano Pirola and José Candido Ferraz.

### **Concerning the editorial changes:**

- 1) We provide a running title: "Inflammation in diabetes and obesity".
- 2) Postcode for the affiliation of co-author JC Ferraz is now provided.
- 3) Contact address and institution for corresponding author L Pirola are now consistent.
- 4) Keywords have been provided. "Obesity; type 2 diabetes; adipose tissue inflammation; crown-like structures; macrophages; eosinophils."
- 5) A "core tip" paragraph is now provided.

"Low-grade inflammation of adipose tissue (AT) contributes to insulin resistance and type 2 diabetes in obese patients. On the contrary, in lean individuals, the immune environment of adipose tissue is non-inflammatory.

In obesity, AT is infiltrated by pro-inflammatory macrophages and T cells leading to the accumulation of IL-1 $\beta$ , TNF $\alpha$ , IL-17 and IL-6.

On the contrary, M2 macrophages, Th2 and T-reg cells producing anti-inflammatory IL-10, IL-5 and IFN $\gamma$ , are present in AT of lean individuals.

Here, we discuss the interaction between AT and infiltrating immune cells in the lean versus the obese condition, with emphasis on the contribution of pro- and anti-inflammatory cytokines to the establishment of insulin resistance."

- 5) An "audio core tip" is now provided.

## **Responses to reviewers.**

### **Reviewer 1 (00004982).**

**The authors described the role of pro- and anti-inflammatory phenomena in the physiopathology of type 2 diabetes and obesity. It is important topic. It would be better to add a summery figure or table regarding the topic.**

We would like to thank the reviewer for the positive appraisal of our manuscript. As suggested, we have now added a summarizing table listing the various immune cell types infiltrating the adipose tissue in the lean and obese condition, with a brief explanation of the produced cytokines and the resulting biological effects.

### **Reviewer 2 (01408945).**

**Manuscript Number: 31581 Manuscript Title: The role of pro- and anti-inflammatory phenomena in the physiopathology of type 2 diabetes and obesity Corresponding Author: Dr. Luciano Pirola The reviewer's critiques are as follows. Major criticism: Nothing. Minor criticism: 1. There are some grammatical errors in English. 2. Authors denote CLS crown-like structures. Authors demonstrated the CLS structures in page 6. It means structures structures.**

We would like to thank the reviewer for the positive evaluation of the manuscript. We have now carefully proofread the manuscript to correct the mistakes pointed out by the reviewers, plus other mistakes present in the original submission.