Reviewer's report

Title: Allograft inflammatory factor 1 (AIF-1) is a new human adipokine involved in adipose inflammation

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Reviewer: Helena Oliveira

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In this study, authors report that AIF-1 is secreted from adipose tissue in a time-dependent manner, mainly by adipose tissue macrophages and that AIF-1 mRNA levels are increased in obese adipose tissue and normalized after weight reduction. In addition, AIF-1 mRNA is inversely correlated with an indicator of insulin resistance. The report is original and relevant to field, in particular to human pathophysiology. The methods are appropriated and data are sound. However, some major points must be addressed, as specified below.

- Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

  - Since mRNA abundance may not reflect the levels of protein and the levels of protein secretion, what was already found for some adipokines (ex. resistin), it is mandatory that the correlation between protein and mRNA levels be well established in a significant number of samples before assuming that mRNA and BMI/KITT correlations represents that adipokine levels are proportional to adipose tissue mass or insulin resistance.

  - Since the main cell type that produces AIF-1 is macrophage, increased AIF-1 must represent increased macrophages infiltration into the adipose tissue and therefore must be correlated to inflammatory markers, either locally or systemically or with a macrophage marker, which may explain an indirect connection with insulin resistance.

  - Acknowledge of the recent close related paper on AIF-1 and metabolic parameters must be done. This paper reinforces present data.


  - Limitations of statistical correlations must be declared, particularly for simple regressions, for adiponectin (correlation that disappear in multiple regression), and for the lack of other relevant metabolic parameters. What happen with BMI in the multiple regression? Is there any independent predictor of AIF-1?

  - Discussion overall is speculative. Indirect connections between AIF-1 and insulin resistance must be reinforced on the basis that AIF-1 is a marker of
activated macrophages.
- The last sentence of conclusions is too speculative.
- Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
- A table with physical and clinical parameters of all subjects (for the 3 cohorts) must be provided, as detailed as possible (sex, age, and BMI, BP, lipids, glucose, insulin, adiponectin, Kitt, etc…)
- Figure legends and descriptions are poorly described. The physical characteristics of the donors of the adipose tissue must be described for each figure (sex, age, and BMI), provide conditioned medium composition, statistical tests in each condition/experiment, including fig 1, etc.
- Fig. 3: paired t test is adequate ONLY for panel C, panel A and B must be UNPAIRED t test
- Table 1 footnote description: explain “delta” meaning, dependent vs independent variables, number of subjects (n).
- Adipose morphology, as described in materials and methods, should be provided.
- English needs revision, ex.: “… were in between” (Results, second paragraph), message in brackets in the first paragraph of Discussion, etc

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests