Reviewer's report

Title: Association of adipocyte genes with ASP expression: a microarray analysis of subcutaneous and omental adipose tissue in morbidly obese subjects

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Reviewer: Javier Gomez-Ambrosi

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The manuscript by MacLaren et al compares the gene expression profile of subcutaneous and omental adipose tissue in obese patients with high ASP and triglyceride concentrations (HAT) vs individuales with low ASP and triglyceride levels (LAT). The work presented is original and interesting, contributing to the better understanding the relation between gene expression in adipose tissue and circulating ASP concentrations and, vice versa, the potential effect of high/low levels of ASP/TG on the genomic of adipose tissue.

Major Compulsory Revisions

1. The microarray study provides evidence of the major (almost exclusive) contribution of subcutaneous adipose tissue in comparison to the omental one on the differences between LAT and HAT. One would expect the opposite, with major alterations in the omental adipose tissue contributing to the higher “lipemic index” in the context of morbid obesity. In this sense, did the authors measure the waist circumference of the patients? However, this finding is only commented in one line in the last paragraph of page 8 and in a merely descriptive way. In my opinion, this is one of the most important findings of the paper and the potential pathophysiological implications of this difference should be better discussed.

2. Expression of the receptor for ASP C5L2 is higher in HAT in comparison to LAT in both the subcutaneous and the omental adipose tissue depots. However, as the authors previously reported, the binding of ASP is significantly higher to the subcutaneous depot (AJP 1999; 26:E815.). How can these findings be reconciled?

3. It must be specified in the conclusion of the abstract and the discussion that the differences are mainly related to the subcutaneous adipose tissue depot.

4. Adipose tissue samples from lean volunteers were obtained during hysterectomy surgery or valve replacement. Do these procedures have an inflammatory component that may be affecting gene expression in adipose tissue? In addition, does the pathophysiology of these diseases may play a role on the gene expression levels? This should be briefly mentioned in the manuscript.

5. Data regarding the expression of IL-4, IL-13 and IL-10 seem not to correspond with the numerical data detailed on sup Table 1 unless the histogram starts on 50%. In my opinion, the scale of the y-axis of every figure should start on 0 in order to be clearer.
6. The ASP triad (FD, C3, and FB) increases in HAT vs LAT, while IL13 tends to decrease. However, they exhibit a significant positive correlation (sup Table 1 and sup fig 3). How is this possible?

Minor Essential Revisions

1. In the second paragraph of “Lipolysis Genes” in the Results’s section it seems that perilipin is referred to as “… other lipases..” However, perilipin limits the access of cytosolic lipases to lipid droplets thus promoting TG storage. This information may be misleading.

2. In the same paragraph, carboxylesterase1 is also named adipose TG lipase. While carboxylesterase1 may be also called triacylglycerol hydrolase, to my knowledge, the name “adipose TG lipase” is more frequently used for PNPLA2 (aka ATGL).

3. Some explanation (although hypothetical) for the decreased expression of FABP2 and 7 (sup Fig 2) should be provided.

4. The sentence (second paragraph of “Differentiation Genes…. in the Results’ section) “…In accordance with decreased expression…” should be amended.

5. In the third paragraph of “Inflammatory Genes” in the Results’ section it should be specified that the information detailed is referred to the subcutaneous adipose tissue depot.

6. Genes regarding panels A and B are interchanged in the legend of figure 4.

Discretionary Revisions

1. ** and *** corresponding to p<0.01 and p<0.001, respectively, is not used in the figure and therefore may be removed from figure 1.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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