Reviewer's report

Title: Altered intestinal functions and increased local inflammation in insulin-resistant obese subjects: a gene-expression profile analysis

Version: 1
Date: 19 June 2015

Reviewer: Adil Mardinoglu

Reviewer's report:

Veilleux et al obtained duodenum specimens from 18 severely obese subjects (BMI # 40 kg/m2), underwent bariatric surgery and investigated the global gene expression differences between IR and IS subjects. The authors matched the sex, age and BMI of the subjects in each group and used the plasma insulin and glucose levels to calculate the HOMA-IR. Total cholesterol, free cholesterol and triglyceride levels have also been measured in the plasma of each patient. Gene expression data have been generated using illumina platform and the expression of the identified target genes have been validated by quantitative real time PCR (qPCR).

Differentially expressed genes were identified as having a false discovery rate (FDR) smaller than 0.05 calculated using the Significant Analysis of Microarrays method. The authors used a total of 195 genes with a fold change greater than 1.2 and with a p value smaller than 0.05 in their metabolic pathway analysis.

Even though, the sample size is quite small, the authors identified differentially expressed genes after multiple testing and validated their result with qPCR. The study is technically and computationally very well executed. The results of the analysis is also interesting. I recommend the acceptance of the manuscript after its revision based on the comments below.

Major Compulsory Revisions:

1) Can you clarify the statement? Even though differentially expressed genes were identified as having an estimated fold-change of at least 1.5, a total of 195 genes with a fold change greater than 1.2 and with a p value smaller than 0.05 were included in the metabolic pathway analysis. What is the reason for using a fold change greater than 1.2 not 1.5?

2) Is there any specific reason for having a cut of 1.2 FC why not 1.1 or 1.3?

3) The authors discussed the differentially expressed genes in the manuscript. I strongly recommend the authors to perform gene enrichment tests using gene ontology biological process terms. (P-values for all of the genes in the array should be used for the enrichment test. Not the ones significantly changed only) There are many tools available for this analyse and it will allow the author to present the global differences between the two groups.
4) The title of the Table 2 should be changed since the authors do not represent the metabolic pathways only. The general understanding about the metabolic pathways are TCA cycle, amino acid metabolism, glycolysis etc. It seems that biological processes are presented in Table 2.

5) The authors had a very nice discussion of their results. It would be also very nice if they discuss the results of GO enrichment analysis.

6) The authors may also measure some of the inflammatory markers in the plasma of the subjects and present if the changes in gene expression are also reflected into the plasma. It would be quite interesting to present this data. Of course this is only possible if they have plasma samples left from the subjects involved in the presented study.

7) I was very much interested in going over the 195 differentially expressed genes in Supplementary Table 1 but I could not get access. It would be great if they can fix it during the revision.

8) Gene expression data should be deposited to GEO database. I am sure it will be used in number of future studies.

9) I also recommend authors to include a table about the characteristics of the involved in the study. Sex, age, BMI, plasma parameters etc.

Evaluation:
1. Is the question posed by the authors well defined?
   Yes
2. Are the methods appropriate and well described?
   Yes
3. Are the data sound?
   Yes
4. Do the figures appear to be genuine, i.e. without evidence of manipulation?
   The authors can improve their figures but they are also ok as it is.
5. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   I recommended the authors to submit their data to GEO database.
6. Are the discussion and conclusions well balanced and adequately supported by the data?
   The authors had a very nice discussion about their results. I do not have any objection if they do not have any space limitation.
7. Are limitations of the work clearly stated?
   The authors included the limitations of their study in to the discussion section.
8. Do the authors clearly acknowledge any work upon which they are building,
both published and unpublished?
To my knowledge, they cited the relevant literature.
9. Do the title and abstract accurately convey what has been found?
   Yes, the title and abstract is appropriate.
10. Is the writing acceptable?
    Yes.

**Level of interest:** An article of outstanding merit and interest 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.