Reviewer's report

Title: Leptin and adiponectin DNA methylation levels in adipose tissues and blood cells are associated with BMI, waist girth and LDL-cholesterol levels in severely obese men and women

Version: 2 Date: 2 February 2015

Reviewer: Yvonne Böttcher

Reviewer's report:

Leptin and adiponectin DNA methylation levels in adipose tissue and blood cells are associated with BMI, waist girth and LDL-cholesterol levels in severely obese men and women.

The study by Houde et al. describes the potential relationship of DNA methylation levels at ADIPOQ and LEP with variables of obesity and obesity-related complications. The authors report that methylation levels at several CpG sites in the ADIPOQ promoter in SAT are positively correlated to BMI, while LEP CpG sites are negatively related to BMI in blood.

Major Compulsory Revisions:

1) Although the authors refer to Reference 30 the pyrosequencing strategy should be included describing the position and architecture of the analyzed CpG sites. Moreover, bisulfite conversion and target sequences should be provided.

2) What is the rational for using paired samples of adipose tissue? Did the authors detect adipose tissue specific variabilities that translate into clinical variables/phenotypes?

3) Why were hyper or hypomethylated CpG sites excluded from the analysis? This need to be addressed.

4) In the Methods 21 CpG sites (LEP) are mentioned and others on ADIPOQ. While repeatedly p-values for CpG7 and CpG11 are presented no data are shown for the other sites. The data should be provided.

5) Page 8, last sentence: It is unclear why a correlation should be estimated between LEP and ADIPOQ. Please re-write the sentence.

6) Did the authors adjust blood derived methylation levels for leukocyte counts?

7) What is the mean methylation level of the CpG islands and is this correlated between the different tissues? Does this translate into clinically relevant parameters of obesity or related co-morbidities?

8) The corresponding m-RNA expression should be presented including the mentioned negative correlation with the respective methylation levels. Is the m-RNA level of ADIPOQ and LEP correlated with clinical phenotypes? Data on m-RNA expression should be included along with interpreting the data in the discussion.
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.