Reviewer’s report

Title: Altered DNA methylation in liver and subcutaneous and visceral adipose tissues derived from individuals with obesity and type 2 diabetes

Version: 1 Date: 10 Dec 2017

Reviewer: Miles C. Benton

Reviewer's report:

I have spent time reading through the authors responses and while I can see that they have attempted to address all comments I feel that several of their responses are a bit cursory. My major criticism would be that the authors haven't provided much additional info or context regarding their study (either in the background or discussion) - meaning that it is currently hard to place it clearly within the current body of literature. I would expect them to have explicitly referenced and mentioned studies in T2D with respect to the different tissues. Where they have allegedly done it, it isn't thorough or specific, for example:

Discussion p11 L21-22 (and their response to minor point 3) - they have added references 18 and 31, after talking about liver and VAT differential methylation in their study. Reference 18 is pancreatic beta cells, whereas 31 is liver. Where are the references for VAT?

Another example is their response to my query about cell mixture (heterogeneity). They take this on board which is great, and they say they have corrected for whole blood (p11 L14), but there is no mention of the tool(s) used to do this, no methodology and no references - this feels more like an appeasement as it currently stands and at the bare minimum there should be methods reported for this procedure.

The authors should be commended for making their data available to the reviewers, and publicly when published. I downloaded the methylation data and checked the comparisons being made between average methylation of tissues (Figure S2). I can corroborate the statistics outlined in the manuscript, however I would suggest a revision of the figure - as it stands it doesn't visually reflect the underlying statistics (attached an example showing clearer distribution of the data), but I will leave this up to Editorial discretion.

In light of the above I still think that this is a very valuable data set and the authors are very close to a publishable manuscript, I believe that there is more detail still required in the manuscript but I will leave the decision to the Editorial team.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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