Reviewer's report

Title: Fatty acid binding protein 3 (FABP3) is associated with insulin, lipids and cardiovascular phenotypes of the metabolic syndrome through epigenetic modifications in a Northern European family population

Version: 2 Date: 14 December 2012

Reviewer: Reid S Alisch

Reviewer's report:

Major Compulsory Revisions:
1. It needs to be clear, at least in your discussion, how to interpret your EMSA data in light of the fact that MetS patients have elevated levels of HFABP. Since the "completely methylated" promoter is not physiologically relevant, as only 2/17 CpG units interrogated were near 100% methylation, while most others 14/15 were less than 40% methylated, perhaps a simple reporter/expression vector system will provide a more thorough dissection of the promoter, especially needed for the claims made by the authors here. Hence, it would be more relevant if you could compare the expression levels of a promoter with 100% methylation at CpG units 20 and 21/22 to a promoter with 0% methylation at those same two sites.

Minor Essential Revisions:
1. Authors need to define the definition of CpG island shores that they are using for this manuscript, as it doesn't meet the conventional of 2000 nucleotides on each side of a CpG island Irizarry et al. 2009).
2. Please state the sensitivity of the assay as many of the differences found are <2%.
3. Define CpG island shores. Irizarry et al. 2009 referred to them as 2000 bp on each side of a CpG island. This definition doesn't seem to fit your description.
4. Combining CpGs as one “unit” may provide a misleading level of methylation at either CpG.
5. In the discussion the authors state: "High levels of correlation in CpG methylation profiles between peripheral blood and other tissue types..." This is overstated and should be modified as CpG methylation is highly tissue type specific.

Level of interest: An article of limited interest

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

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I have not competing interests.