Reviewer's report

Title: MicroRNA-125a is overexpressed in insulin target tissues in a spontaneous rat model of Type 2 Diabetes

Version: 2 Date: 20 April 2009

Reviewer: David Arthur Carlyle Simpson

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Discretionary Revisions

The amendments made by the authors have improved the manuscript and the changes in the discussion will assist in interpretation by the reader. The authors have generally addressed the previous comments, as outlined in the same order below:

1. The authors have clarified the rationale for the choice of the BN rat as the control. The penultimate sentence in the discussion now makes the significance of the findings for future studies clear.

2. The authors have addressed this comment by including a paragraph in the Discussion which acknowledges the strain differences and the desirability of supporting evidence from other models.

3. The change in analysis has addressed this comment.

4. The authors have fully addressed this comment regarding enrichment of miR-125a target genes and performed the suggested analyses, which I am pleased to see have yielded some useful information. The relationship between change in miR125a expression and predicted target gene enrichment is weak (not detected for Targetscan or PicTar) and rather confusing (more overlap in adipose which has a lesser fold change; enrichment amongst upregulated genes). This is perhaps not surprising given the difficulty of target gene prediction and the many influences on gene expression in the diabetic condition. It would be helpful to mention these issues in the discussion.

Additional comments:

1. The validation of the change in expression of miR-125a by qRT-PCR has strengthened the data.

2. In the amended supplementary table 2 what does red and blue colouring denote? If genes altered within a particular pathway are changed in different directions, can the authors comment on how this should be interpreted.

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'