Reviewer’s report

Title: Role of Receptor-Interacting Protein 140 in Human Fat Cells

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Reviewer: Stuart Wood

Reviewer’s report:

In this manuscript, the authors have described Receptor-interacting Protein 140 (RIP140) in human adipose tissue and isolated adipocytes. They have shown the presence of RIP140 protein and in human white adipose tissue. Gene expression was increased during differentiation of preadipocytes to mature adipocytes. Furthermore RIP140 mRNA levels were decreased in adipose tissue isolated from obese subjects compared to lean. Finally, their results have suggested that RIP140 inhibits glucose uptake and genes involved in energy expenditure.

Overall, the work is of interest. However, the paper has raised a number of issues which are described herein.

Major Compulsory Revisions

1. With respect to the effect of RIP140 knock down on glucose transport, why did the authors collect the cells used for gene expression analysis at 48 h and the uptake experiment conducted at 72 h?

GLUT1, although expressed at low levels is the predominant basal glucose transporter and GLUT4 is sequestered as an intracellular pool which plays a major role in glucose uptake following insulin signalling. Any change in basal glucose uptake would be expected to derive from effects on GLUT1 expression. Are the authors suggesting that increased in GLUT4 expression results in the increased insertion of GLUT4 in the plasma membrane in the basal state? This experiment would have been strengthened by the inclusion of GLUT1 and GLUT4 protein analysis. If no change in GLUT1 levels could there be post-translation effects on GLUT1 protein or other GLUT proteins involved (other than GLUT4)?

2. It is not clear from the data whether there was insulin-stimulated glucose uptake in the scramble SiRNA transfected cells. The error bars appear very large. This would need to be assured within the experiment to make the finding with the insulin-stimulated knock-down RIP140 cells valid.

3. p12, results, para1 – what was the extent of the difference between the cohorts described in fig 1?

4. Fig3 – the signal strength for RIP140 appears to be highly variable both inter- and intra- samples of those subjects analysed. This would benefit from the inclusion of a loading control. Furthermore, letterboxing of the western blot image
should be dissuaded.

5. The error bars on figures 1, 2, and 4 appear to be very large and it is difficult to see how significance is reached in most cases.

Minor Essential Revisions

p8,p22 - Undifferentiated adipocytes = preadipocytes?
p15 – change the term marginally significant. It is either significant or it is not.

Discretionary Revisions

p14 – “RIP140 is more abundantly expressed in ....” – substitute “enriched” for “more abundantly”? ie “RIP140 expression is enriched in isolated fat cells compared to intact WAT.”

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests