

RESPONSE TO REVIEWERS

Authors: We wish to thank the reviewers for their helpful suggestions.

Reviewer

The paper by Arcidiacono and coauthors is interesting. It reports data on MMP-11 expression in murine cell culture and in an animal model of insulin resistance. They show that MMP-11 is upregulated under that condition, causing dysregulation of ECM, and contributing to the onset of obesity.

The paper is straightforward, well written, and it adds novel information on the topic. I think it should be accepted for publication.

However a major problem should be addressed: figure 3 seems wrong, indeed it shows that mice on a low-fat diet have insulin resistance. The authors should explain.

Minor: some typing errors should be corrected (i.e., line 238 “expresion”...)

Authors: Concerning Figure 3, we apologize for the oversights in the previous version of this figure, which have now been amended (see new Figure 3).

Typing errors have been corrected.

Reviewer

The aim of this study was to examine the effect of insulin resistance on the expression of MMP-11 in the adipose tissue. The study was performed in vitro using 3T3-L1 adipocytes as well as in vivo in mice made obese by high fat diet applied for 15 weeks. It is demonstrated that: 1) the expression of MMP-11 increases during preadipocyte to adipocyte differentiation, 2) hypoxia and/or TN-alpha increase the expression of MMP-1 in 3T3-L1 cells, 3) the expression of MMP-11 in white adipose tissue is higher in obese than in lean mice which is accompanied by up-regulation of several markers of fibrosis. The results are of interest and the manuscript is quite well-written. Nevertheless, there are some issues which should be addressed. 1) It should be specified in the Abstract what was actually measured (MMP-11 mRNA or protein). 2) Which WAT depot was used for the measurement of MMP-11? 3) Why only mRNA but not MMP-11 protein was measured in vivo? 4) The results are rather descriptive. Neither the mechanism nor the consequences of MMP-11 up-regulation have been elucidated in this study.

Authors:

1) It is now clarified in the abstract that MMP-11 expression was assessed at the mRNA level (see lines 84 and 90);

2) It is now specified that epididymal white adipose tissue was used to measure MMP-11 expression in vivo, in whole animal (see Material and Methods section, Animals paragraph, line 238).

3) We are aware that ex-vivo data on MMP-11 protein expression would have strengthened our findings; however, we were unable to achieve a sufficient protein yield to carry out western blot analyses.

4) We now refer to this point (see Discussion section, end of second paragraph, lines 327-330).