Author's response to reviews

Title: Adiponectin, chemerin, cytokines, and dipeptidyl peptidase 4 are released from human adipose tissue in a depot-dependent manner: An in vitro system including human serum albumin

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Version: 4 Date: 9 January 2014

Author's response to reviews: see over
Dear Professor Shipley,

Thank you for the second review of our manuscript “Adiponectin, chemerin, cytokines, and dipeptidyl peptidase 4 are released from human adipose tissue in a depot-dependent manner: An in vitro system including human serum albumin” (MS: 2127760056103508). We are pleased to hear that our revision fulfilled wishes and requirements from Reviewer 2. Please find below a point-by-point response to the remaining concerns raised by Reviewer 1.

We hope that the manuscript will now be acceptable for publication in BMC Endocrine Disorders.

Sincerely yours,

Malin Lönn, PhD
Associate professor
Reviewer comments:

1. The main concern of the revised manuscript is that it does not address the point regarding the effect of the increased LPS amount reported in BSA compared with the low LPS concentration. In the previous review I propose to test several LPS concentrations as a negative control. Since, the effects of LPS could not be exclude, I suggest another way to test this point. Currently, there are available of commercial BSA-entotoxin free, this BSA should be used in the comparative study with HSA.

Again, we would like to thank Reviewer 2 for the inspiration to initiate experiments with the aim of exploring the mechanism behind BSA induction of cytokine release. However, for us, this is clearly the scope of a future investigation. As stated in the abstract, the aim of the present study was “to compare release of a number of adipokines/cytokines – all implicated in insulin resistance – from human subcutaneous and visceral AT in a short-term incubation system minimizing cytokine induction and including repeated measurements during 24h”.

Using our incubation protocol including HSA, cytokine induction was indeed minimized, while two commonly used BSA preparations markedly induced cytokine release.

Further, as stated in the Discussion (line 269), our results suggest that this effect of BSA may be mediated by a high concentration of endotoxin although immunomodulatory effects of albumin, not due to endotoxin contamination, has also been reported (Wheeler DS, Giuliano JS, Jr., Lahni PM, Denenberg A, Wong HR, Zingarelli B: The immunomodulatory effects of albumin in vitro and in vivo. Advances in pharmacological sciences 2011, 2011:691928). Thus, the mechanisms behind BSA induction of cytokine release from human adipose tissue, with its diverse cell composition, are likely to be complex and (again) beyond the aim of the present study.

2. Have the authors compared the effects of BSA and HSA in other cell model, such as 3T3-L1?? I think that this is necessary to confirm that these differences are only in human preadipocytes.

The present manuscript, as well as all our investigations at present, are focused on human adipose tissue. However, other authors report that BSA promotes IL-1β and TNF-α secretion by microglial cells suggesting that this effect of BSA is not specific for human adipose tissue or human primary adipocytes (Zhao TZ, Xia YZ, Li L, Li J, Zhu G, Chen S, Feng H, Lin JK: Bovine serum albumin promotes IL-1beta and TNF-alpha secretion by N9 microglial cells. Neurol Sci 2009;30:379).

We recommend that for any in vitro system for human adipose tissue or adipocytes, potential albumin effects on tissue/cell function should be considered. This has now been added to the Conclusion (line 347). The focus on human adipose tissue in the present study has also been clarified in the last sentence of the Abstract (line 56).