Reviewer’s report

Title: IL-10/STAT3 is reduced in childhood obesity with hypertriglyceridemia and is related to triglyceride level in diet-induced obese rats

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Reviewer: Michaela Siklova

Reviewer's report:

The authors investigated the association of IL-10 mRNA expression in adipose tissue (AT) with TG and FFA levels children. Further, in rats the expression (mRNA and protein) of IL-10, STAT and ATGL was analyzed during the long-term feeding period (8th-24th week of age) together with FFA, TG and IL-10 plasma levels. The effect of obesity (high-fat diet) was compared to control diet. The study is acceptably conducted, however, several important analyses are missing, the discussion of results and conclusions are not appropriate.

Main points:

1) The main heading is probably not grammatically correct. This should be changed.

2) It is not clearly explained, why the authors have chosen IL-10 as a candidate cytokine influencing the adipose tissue (AT) metabolism. The clarification of the study in the introduction (page 4, row 13-30) is general and vague. The possible role of IL-10 in AT metabolism should be more specified. Moreover the authors do not explain in the introduction, why they focused on STAT and ATGL expression in AT. How these genes were chosen and why just these two in AT metabolism??

3) The authors show the effect of obesity on IL-10, STAT and ATGL expression in rats. Is it also true in human part of study? Why these factors (at least on mRNA level) were not measured in AT in children?

4) The secretion of IL-10 from AT into the plasma AT is discussed in rats (row 58-59). Thus, the measurement of plasma values of IL-10 in children population would be suitable.

5) Adiponectin and leptin were measured in plasma of the children population, these data are not discussed. IL-10 expression in AT might be associated with adipokines production. Did you find any correlation of IL-10 with adiponectin or leptin?
6) In Results and in Discussion section is mentioned several times that the levels of IL-10, STAT and ATGL are "higher" after 8 weeks of feeding. It is not possible to comment the results in this way, if the statistical significance was not reached!! Also according to the standard errors in some cases, only no change may be concluded!

7) There is stated in the discussion (page 7, row 55-57) that the levels of IL-10 negatively correlated with systemic lipolysis in rats, however, there are no such correlations shown in the paper. Moreover on the page 8, row 33 is stated that "ATGL may be related to the decrease of IL-10". Are there any correlations between changes in IL-10 expression and ATGL or STAT expression?

8) The authors conclude that IL-10 might play an important role in triglyceride metabolism by regulation of ATGL (page 8, row 57,58) and that show "evidence that JAK-STAT pathway is dysfunctional in triglyceride metabolism in obese rats" (page 8, row 40,41). However, this is no functional study or study using knock-out model of the mouse. This conclusions are not appropriate!! The results show only similar profile of the expression of IL-10, STAT and ATGL. Even if there would be correlation, it may be consequence of obesity - dysfunction of AT, changes in metabolic profile or immune cells profile. The association between the measured variables might be hypothesized, but no direct regulation is shown. Moreover, only few factors included in the signalization and AT metabolism/lipolysis were analyzed.

9) It was shown in recent study that Aglistatin administration improves obesity-associated metabolic complications in obese mice by decreasing lipolysis through ATGL lowering (Schweiger et al., Pharmacological inhibition of adipose triglyceride lipase corrects high-fat diet-induced insulin resistance and hepatosteatosis in mice. Nat Commun. 2017 Mar 22;8:14859). However, the present study shows importantly decreased ATGL expression in association with increased FFA and TG in obese rats (thus increased lipolysis). Please discuss more in detail this discrepancy (row 25, 26).

Minor points

10) The statement in the abstract about FFA and TG measurement should be corrected. It was definitely not analyzed by ELISA.

11) In the methods (page 5, row 32) the number of animals sacrificed and analyzed at the end of the study (24th week) should be clearly stated.

12) The abbreviation "SD" (page 5, row 8) is not previously clarified in the text. Please expand.
13) Table 1- the abbreviation (variable) SDS-BMI is not clear. Please explain in the methods or under the table.

14) Statistical analysis using Two-way ANOVA or appropriate non-parametric multiple regression model would be more suitable, as the values in more time points are compared in the two groups of rats.

15) It should be stated in the figure legend, if the data are presented as mean ± SD or mean ± SEM.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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