

## Peer Review File

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### Reviewer A

Comment 1: Title

It should mention the fact that all the work is done in a murine model, the word “children” is confusing...

Reply 1: Thank you for your advice. We've changed the “children born small for gestational age” into “rats born small for gestational age”.

Changes in the text: Please see line 3, line 29, line 38, line 41 and line 50.

Comment 2: Introduction

This section is clear.

Reply 2: Thank you!

Comment 3: Methods

I would suggest a reorganization of the paragraphs, with some kind of chronological logic, allowing a better understanding for clinicians... For example, tolerance tests procedures should appear just after establishment of animal model and ATM and hepatocytes isolation procedures should appear before exosome isolation.

Reply 3: Thank you for your advice. We've adjusted the chronology.

Changes in the text: Please see line 140-174.

Comment 4: A sentence explaining why phospho-AKT is used as a marker for insulin signaling would be useful.

Reply 4: Insulin resistance is mediated by the phosphorylation of AKT.

Changes in the text: Please see discussion line 404.

Comment 5: Results

All legends should be revised, avoiding descriptive sentence order. For example, Figure 1 (A-E) should become ‘comparison of fasting blood glucose levels... in CUG-SGA and AGA rats’.

Reply 5: Thank you for your advice. We've revised the legends in Figure 1 (A-E).

Changes in the text: Please see line 537-539.

Comment 6: Figure 2: A B and F are not easily readable and should be larger

Reply 6: Thank you for your advice. Figure 2: A B and F had been amplified.

Changes in the text: Please see line 553-554.

Comment 7: Figure 3: what is the difference between label B and C

Reply 7: Thank you for your advice. We've revised the Figure 3 B and C.

Changes in the text: Please see line 570.

Comment 8: Figure 4: should be reorganized in order to put label B, C and D on the same line, and just over label E, F and G (maybe inverting label B and H)

Reply 8: Thank you for your advice. We've revised the Figure 4.

Changes in the text: Please see line 580-587.

Comment 9: Figure 5: should be reorganized in order to put label C, D and E on the same line (maybe inverting label C and F)

Reply 9: Thank you for your advice. We've revised the Figure 5.

Changes in the text: Please see line 597-603.

Comment 10: Discussion

This section is clear.

Reply 10: Thank you!

## Reviewer B

1. Highlight box:

Do not describe the same contents (below yellow parts) in the Highlight box. Please revise.

36 **Key findings**↵

37 Adipose tissue macrophage-derived exosomal microRNA (miR)-210-5p modulates  
38 insulin sensitivity in rats born small for gestational age with catch-up growth by  
39 targeting SID1 transmembrane family member 2 (*SIDT2*).↵

40 ↵

41 **What is known and what is new?** ↵

42 ● miR-210-5p is markedly upregulated in the exosomes derived from adipose tissue  
43 macrophages (ATMs). miR-210-5p in exosomes derived from high glucose-  
44 induced macrophage RAW264.7 cells inhibited glucose uptake and mitochondrial  
45 complex IV (CIV) complex activity in 3T3-L1 adipocytes.↵

46 ● Adipose tissue macrophage-derived exosomal miR-210-5p modulated insulin  
47 sensitivity in rats born small for gestational age with catch-up growth by targeting  
48 SIDT2.↵

Reply 1: Thank you for your advice. We've revised the same contents.

Changes in the text: Please see line 37-39.

2. Please check all abbreviations in the main text, such as below. **All abbreviated terms should be full when they first appear.**

157 and L6 myocytes were incubated with 100 nM of insulin for 30 min at 37 C°. Cells

158 were washed twice with PBS, and 1 mM of 2-deoxyglucose (2DG) was added and

169 centrifuged at 500 rpm for 5 min at 4 C°. Finally, cells were resuspended and seeded

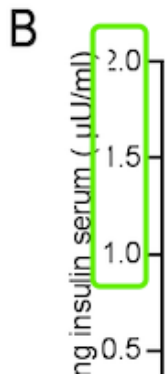
170 onto a 6-well plate in DMEM containing 10% FBS. ↵

Reply 3: Thank you for your advice. We've revised these all abbreviated terms.

Changes in the text: Please see line 156, line 169.

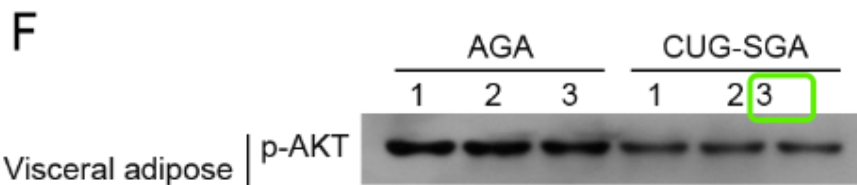
3. Figure 1:

1) Figure 1B: the numbers in the y-axis are not complete and not clear. Please revise.



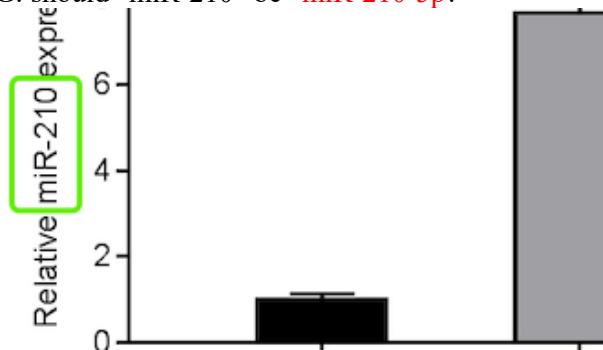
Reply 6 1): Thank you for your advice. We've revised the numbers in the y-axis in Figure 1B. Changes in the text: Please see line 549.

2) Figure 1F: the group 3 is in the wrong place. Please modify.



Reply 6 2): Thank you for your advice. We've modified the group 3 in Figure 1F. Changes in the text: Please see line 550.

3) Figure 1G: should "miR-210" be "miR-210-5p"?



Reply 6 3): Thank you for your advice. We have changed "miR-210" to "miR-210-5p" in Figure 1G. Changes in the text: Please see line 551.

4) There is no \*\* in Figure 1 but you indicated it in the legend. Please check.

Reply 6 4): Thank you for your advice. We have checked and modified it in Figure 1. Changes in the text: Please see line 557.

4. Figure 2:

1) Please indicate the magnification or scale bar in Figure 2F legend.

Reply 7 1): Thank you for your advice. We have indicated the scale bar in Figure 2F. Changes in the text: Please see line 561.

2) There is no \* in Figure 2 but you indicated it in the legend. Please check.

Reply 7 2): Thank you for your advice. We have checked and modified it in Figure 2. Changes in the text: Please see line 572.

8. Figure 3:

There is no \*, \*\*, \*\*\* in Figure 3 but you indicated it in the legend. Please check.

Reply 8: Thank you for your advice. We have checked and modified it in Figure 3. Changes in the text: Please see line 584.

5. Figure 4:

1) Please check the citation of Figure 4 in your main text. Figure 4C-E appears earlier than Figure 4B in your text, which is not allowed. Figures should be cited consecutively in the text and numbered in the order in which they are discussed. (For example: Figure 1 contains 4 parts, such as Figure 1A, 1B, 1C, 1D, these parts should also be cited consecutively, unless Figure 1 is already cited before Figure 1A, 1B, 1C, 1D.).

Reply 9 1): Thank you for your advice. We have written in the order of the revised figure 4.  
Changes in the text: Please see line 326-335.

2) There is no \*, \*\* in Figure 4 but you indicated it in the legend. Please check.

Reply 9 2): Thank you for your advice. We have checked and modified it in the Figure 4.  
Changes in the text: Please see line 601.

6. Figure 5:

1) Please check the citation of Figure 5 in your main text. Figure 5D-F appears earlier than Figure 5C in your text, which is not allowed. Figures should be cited consecutively in the text and numbered in the order in which they are discussed. (For example: Figure 1 contains 4 parts, such as Figure 1A, 1B, 1C, 1D, these parts should also be cited consecutively, unless Figure 1 is already cited before Figure 1A, 1B, 1C, 1D.).

Reply 10 1): Thank you for your advice. We have written in the order of the revised figure 4.  
Changes in the text: Please see line 326-335, and line 592-600.

2) There is no \*, \*\*, \*\*\* in Figure 5 but you indicated it in the legend. Please check.

Reply 10 2): Thank you for your advice. We have checked and modified it in the Figure 5.  
Changes in the text: Please see line 615.

3) Please indicate the meaning of ##### in Figure 5 legend.

Reply 10 3): Thank you for your advice. We have checked and modified it in the revised Figure 5.  
Changes in the text: Please see line 607.

7. Figure 6:

1) There is no \*, \*\*, \*\*\*, #, #### in Figure 6 but you indicated it in the legend. Please check.

Reply 11 1): Thank you for your advice. We have checked and modified it in the Figure 6.  
Changes in the text: Please see line 626-628.

2) Please indicate the meaning of ##### in Figure 6 legend.

Reply 11 2): Thank you for your advice. We have modified it in the revised Figure 6.  
Changes in the text: Please see line 619.