

Ref: YCLNEX\_2018\_9

Title: Growth Factors Profile in Conditioned Medium human Adipose Tissue-derived Mesenchymal Stem Cells (CM-hATMSCs)

Journal: Clinical Nutrition Experimental

Dear Dr. Widowati,

Thank you for submitting your manuscript to Clinical Nutrition Experimental. I have completed the review of your manuscript and a summary is appended below. The reviewers recommend reconsideration of your paper following major revision. I invite you to resubmit your manuscript after addressing all reviewer comments. You may also submit it as a short communication.

When resubmitting your manuscript, please carefully consider all issues mentioned in the reviewers' comments, outline every change made point by point, and provide suitable rebuttals for any comments not addressed.

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I look forward to receiving your revised manuscript as soon as possible.

Kind regards,

Professor Singer  
Editor-in-Chief  
Clinical Nutrition Experimental

**Comments from the editors and reviewers:**

**-Reviewer 1**

-

The authors investigate the growth factor profile in CM-hATMSCs and concludes that FGF is the most important modulator released. This preliminary study is of potential interest in the field of regenerative medicine, however this reviewer has some concerns regarding the publication of the manuscript.

English language must be thoroughly revised throughout the paper, as several passages are difficult to understand in the present form.

Sample were collected from only 3 donors and therefore the study appears very preliminary and should be reinforced to meet adequate statistical power. Also,  $n=3$ , does not allow for data to be presented as  $\text{mean} \pm \text{sd}$ , nor for an appropriate use of ANOVA, post-hoc tests or t-tests. Dots for single measurements should be used in graphs.

Data presentation is not appropriate. Figure 1 and 2 are unnecessary and duplicate data presented in figure 3. Instead the authors could show the difference in growth factor secretion between FFP and non FFP treatment.

The discussion section is more an introduction to the role of the measured growth factor than a discussion of obtained results.

Importantly, as FGF shows the higher concentrations, the authors conclude it is the main effector in CM-related regenerative effects and that it could be used in anti-aging products. This conclusion is unsupported by any experimental evidence. Moreover, FGF levels are high also in non FFP treated samples. Importantly, how can the authors state that higher absolute concentrations of any molecule are related to its prominent biological role and to higher effects compared to other factors? Authors should completely revise their conclusions.

**-Reviewer 2**

-

Noverina and Colleagues report on growth factors in conditioned medium from adipose tissue-derived stem cells with or without treatment with frozen plasma. They observe that fibroblast growth factor is the highest component from the medium under both treatment

conditions. The authors then conclude that FGF as derived from adipose tissue stem cell conditioned medium has potential for wound healing and cell regeneration and that it can be used in anti-aging products. Although the research question is potentially interesting, several relevant concerns need to be addressed:

- 1) Since Figure 1 and 2 are recapitulated in Figure 3, the amount of information reported is limited. This should be reorganized and submitted as a short-communication or a letter with shortening of all sections, unless the authors may provide additional experiments investigating additional regulatory incubation conditions from more subjects.
- 2) The conclusion that FGF has potential for wound healing and cell regeneration, or that it can be used in anti-aging products, cannot be inferred by the current very limited experiments.
- 3) Some additional characteristics of human cell donors should be provided.
- 4) Language revision is needed.

Ref: YCLNEX\_2018\_9\_R1

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I look forward to receiving your revised manuscript as soon as possible.

Kind regards,

Professor Singer  
Editor-in-Chief  
Clinical Nutrition Experimental

**Comments from the editors and reviewers:**

**-Reviewer 1**

- The authors have partially improved the manuscript. However, the study remains preliminary. Data analysis and presentation could still be improved, as parametric statistics is not appropriate. This reviewer must point out that, given the low independent sample number, data and conclusions should at least be declared as preliminary in the discussion and conclusions sections.

**-Reviewer 2**

-

Some improvements have now been achieved following previous recommendations. Given the structure of experiments, I would recommend that the authors explicitly state in the title, discussion and conclusion that this is a preliminary or pilot experiment.

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Dear Dr. Widowati,

Thank you for submitting your revised manuscript for consideration for publication in Clinical Nutrition Experimental. Your revision was received in good order.

To track the status of your manuscript, please log into EVISE® [http://www.evise.com/evise/faces/pages/navigation/NavController.jspx?JRNL\\_ACR=YCLNEX](http://www.evise.com/evise/faces/pages/navigation/NavController.jspx?JRNL_ACR=YCLNEX) and locate the submission under the header 'My Submissions with Journal' on your 'My Author Tasks' view.

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Clinical Nutrition Experimental

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## RESPOND TO REVIEWERS

### On Article entitled “Growth Factors Profile in Conditioned Medium human Adipose Tissue-derived Mesenchymal Stem Cells (CM-hATMSCs)”

#### Reviewer 1

1. The authors investigate the growth factor profile in CM-hATMSCs and concludes that FGF is the most important modulator released. This preliminary study is of potential interest in the field of regenerative medicine, however this reviewer has some concerns regarding the publication of the manuscript.

English language must be thoroughly revised throughout the paper, as several passages are difficult to understand in the present form.

Respond :

Thank your for your comment, we have corrected the the english writings as suggested

2. Sample were collected from only 3 donors and therefore the study appears very preliminary and should be reinforced to meet adequate statistical power. Also,  $n=3$ , does not allow for data to be presented ad  $\text{mean} \pm \text{sd}$ , nor for an appropriate use of ANOVA, post-hoc tests or t-tests. Dots for single measurements should be used in graphs.

Respond :

Thank you for your comment on our article. We only used 3 donors however we conducted this study with many treatments such as treatment with FFP and non FFP also treatment in many passages, but we only use passage 3, 7, 11 and 15 as they have significant different among others.

3. Data presentation is not appropriate. Figure 1 and 2 are unnecessary and duplicate data presented in figure 3. Instead the authors could show the difference in growth factor secretion between FFP and non FFP treatment.

Respond :

Thank you for your comment. We have corrected the figures as you suggested.

4. The discussion section is more an introduction to the role of the measured growth factor than a discussion of obtained results.

Respond :

Thank you for your comment. We have corrected the the discussion as you suggested

5. Importantly, as FGF shows the higher concentrations, the authors conclude it is the main effector in CM-related regenerative effects and that it could be used in anti-aging products. This conclusion is unsupported by any experimental evidence. Moreover, FGF levels are high also in non FFP treated samples. Importantly, how can the authors state that higher absolute concentrations of any molecule are related to its prominent biological role and to higher effects compared to other factors? Authors should completely revise their conclusions.



Respond :

Thank you for your comment. We have corrected the conclusion as you suggested

## **Reviewer 2**

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1) Since Figure 1 and 2 are recapitulated in Figure 3, the amount of information reported is limited. This should be reorganized and submitted as a short-communication or a letter with shortening of all sections, unless the authors may provide additional experiments investigating additional regulatory incubation conditions from more subjects.

Respond :

Thank you for your comment. We have corrected the figure as you suggested. As for our study we used many treatment such as treatment with FFP and non FFP also treatment in many passages, but we only use passage 3, 7, 11 and 15 as they have significant different among others, and so we thought that our data was enough.

2) The conclusion that FGF has potential for wound healing and cell regeneration, or that it can be used in anti-aging products, cannot be inferred by the current very limited experiments.

Respond :

Thank you for your comment. We have corrected the conclusion as you suggested.

3) Some additional characteristics of human cell donors should be provided.

Respond :


Thank you for your comment. We have added characteristics of human cell donors in introduction section.

4) Language revision is needed.

Respond :

Thank you for your comment. We have revised our english writing based on suggestion.

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