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Reviewer 1

Q: In the section possibility of organismic rejuvenation in page 9, factors and agonists are not clearly described. Negative factors and positive factors described in this section should be specified. Please re-check references and section names carefully.

A: I added the following paragraph in this section;

'Examples of negative (pro-aging) factors are p16INK4a, TGF- β and TNF- α , and positive (anti-aging) factors are Notch/Delta and Wnt pathways. We will discuss about the details later in this section.'

Reviewer 2

No Qs

Reviewer 3

No Qs

Reviewer 4

Q1: Paragraph 1 of the introduction should include references.

A: Added corresponding reference.

Q2: History of Rejuvenation Research: Description of the study by Carlson et al does not have an in text citation.

A: Cited [5].

Q3: Targeted Signals Controlling Age Phenotype: Reference 10 is not formatted.

A: Corrected.

Q4: Plasma Fractions/Factors Controlling Age Phenotype: It is not clear whether the authors imply that interleukin 15 neutralizes CCL11. Last sentence

of this section is vague. What do the authors mean by "escape from only investigating serum or plasma fractionation"? What else should be done?

A: Added the phrase 'which is reduced by interleukin 15,' in the sentence.

Corrected last sentence as follows;

'will narrow the search so researchers can focus on not only investigating serum or plasma fractionation, but also molecules and agents that affect the aging/rejuvenation process.'

Reviewer 5

Q: To facilitate the reading and comprehension of the manuscript, I just want to suggest to the Author to draw a scheme showing the main signalling pathways involved in the aging process and described in the text as possible targets of the "rejuvenating strategies".

A: Made Figure 1 and added the corresponding sentence of 'Figure 1 illustrates the possible targets for rejuvenating strategy in aging stem cells.' in the last paragraph of the Conclusion section.

Reviewer 6

Q: Only a few minor corrections are needed, and these can be done by the journal editors.

A: Please do it by journal editors.