

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Aleksei Mikhailchenko

PhD Program: Life Sciences

Title of Thesis:

COMPARATIVE BIOLOGY OF AGING THROUGH THE LENS OF INDUCED PLURIPOTENT STEM CELLS

Supervisor: Prof. Philipp Khaitovich

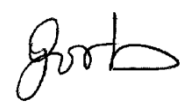
Co-Supervisor: Prof. Vadim Gladyshev

Chair of PhD defense Jury: Prof. Olga Dontsova

Email: o.dontsova@skoltech.ru

Date of Thesis Defense: 23 October 2018

Name of the Reviewer:

<p>I confirm the absence of any conflict of interest</p> <p>(Alternatively, Reviewer can formulate a possible conflict)</p>	<p>Signature:</p>  <p>Date: 07-10-2018</p>
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The purpose of this report is to obtain an independent review from the members of PhD defense Jury before the thesis defense. The members of PhD defense Jury are asked to submit signed copy of the report at least 30 days prior the thesis defense. The Reviewers are asked to bring a copy of the completed report to the thesis defense and to discuss the contents of each report with each other before the thesis defense.

If the reviewers have any queries about the thesis which they wish to raise in advance, please contact the Chair of the Jury.

Reviewer's Report

Reviewers report should contain the following items:

- Brief evaluation of the thesis quality and overall structure of the dissertation.
- The relevance of the topic of dissertation work to its actual content
- The relevance of the methods used in the dissertation
- The scientific significance of the results obtained and their compliance with the international level and current state of the art
- The relevance of the obtained results to applications (if applicable)
- The quality of publications

The summary of issues to be addressed before/during the thesis defense

Thesis by Aleksei Mikhailchenko describes a substantial body of work addressing mechanisms contributing to naked mole rat longevity. The research covers three topics: (1) generation and characterization of naked mole rat iPSCs; (2) generation of rat iPSCs and age-related changes in mouse/rat chimeras; (3) thermogenesis in the naked mole rat. The thesis is well structured and containing appropriate Introduction and discussion sections for each chapter.

The research is highly relevant to the topic of the thesis focusing on comparative biology of the naked mole rat utilizing iPSCs approach. The research uses state-of-the-art methodology such as generation of iPSCs, RNAseq and other analyses.

The results obtained are significant in several ways. Generation of naked mole rat iPSCs is highly significant for research into naked mole rat longevity. It also identifies unique features of naked mole rat iPSCs provide are also significant. Such as resistance of these cells to teratoma formation provides clues for naked mole rat cancer resistance.

The dissertation work resulted in two publications. Both publications appeared in highly respected journals: Stem Cell Reports and Stem Cell Research. Both papers are of high scientific quality and originality.

The following questions need to be addressed in the text:

1. Specify whether iPSCs were generated from LT-immortalized cells. It is stated that embryonic fibroblasts were immortalized, while whether the other cells contained LT is unclear.
2. Elaborate on the unexpected finding of wide spread tetraploidy in naked mole rat iPSCs. Was it connected to LT antigen?
3. Since aborted embryos has higher percentage of naked mole rat cells, does it indicate the difficulty in forming full-term chimeras? What may be the reason?

Provisional Recommendation

I recommend that the candidate should defend the thesis by means of a formal thesis defense

I recommend that the candidate should defend the thesis by means of a formal thesis defense only after appropriate changes would be introduced in candidate's thesis according to the recommendations of the present report

The thesis is not acceptable and I recommend that the candidate be exempt from the formal thesis defense