

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Aleksei Mikhalchenko

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: Olga Dontsova

<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: 03-10-2018</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

Dissertation contains abstract, that describes the work very clearly. The next is literature review that describes major objects of further experimental research: naked mole rat (NMR) and iPSC. Both parts are well written and describes the subject with all necessary details that allows further understanding of the results that were obtained by Alexei Mikhalchenko. The experimental part consists of several chapters each contains short introduction, results, materials and methods and discussion. These parts are devoted to the description of NMR iPSC generation and comparison with mouse and human; generation and investigation of mouse-NMR chimeras and finally research on thermoregulation specific NMR features. The final discussion part is very well written and allows to make a clear link between experimental parts and determine the place of this particular research in the world achievements in the field.

The topic of the research is very relevant and very actual. It is a dream of human being to understand why some species live longer than the others to understand the molecular basis for that and to increase healthy life span. Naked mole rat lives much longer than its close relative mouse. The model of NMR genome was first sequenced by Prof. Gladyshev, the thesis supervisor, who has a priority in the research in the field.

The particular task of this work to generate the iPSC from NMR and compare it with mouse and human and at the next step to generate mouse-NMR chimeras and to follow the fate of iPSC. The applicant successfully got the iPSC from NMR, although in parallel, similar efforts were published by the other group. However Alexei was able to get number of interesting results with iPSC and chimeras that allowed him to be the first author (equal contribution) in two publication in high impact journals (more than 7.4 and 4.5).

During his experiments the applicant not only used wide spectrum of modern techniques, but created novel procedure for NMR iPSC generation. The quality of the experiments is very high and experimental data supports author's conclusions.

No doubts that the results of this study will be very interesting for broad scientific community and especially in the field of age-related research.

The work was published with equal contribution as a first author in two high impact international journals

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