

## 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

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**Date of Thesis Defense:** 23 October 2018

**Name of the Reviewer:**

I confirm the absence of any conflict of interest	<b>Signature:</b>  <b>Date: 09-09-2018</b>
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### Reviewer's Report

The submitted dissertation results from a strong a solid research project, although its composition is somewhat unusual — essentially it is a collection of three largely independent chapter, each structured like a paper. Although there is a common introductory chapter with two main sections dedicated to the biology of the naked mole rat (NMR) and to induced pluripotent cells, each chapter starts with its own introduction, followed by results, discussion, and methods. Of the three research chapters, one (Ch. 2) coincides with one of the published papers, one more published paper deals with a related topic describing generation of the cell line for this research; whereas Ch. 3 is sort of preliminary towards a larger goal of creating a chimera between mouse (short-lifespan mammal) and NMR (long-lifespan creature), describing instead mouse–rat (the latter being neither “naked” nor “mole”) chimeras as a proof of principle; and, finally, Ch. 4 is dedicated to the thermoregulation in NMR, claimed to be linked to its long lifespan. While all this is sort of convoluted, all formal requirements of SholTech are satisfied.

That said, the dissertation is a good one. The introductory chapter and paragraphs are well-structured, with clear underlying logic, and provide a complete coverage of the relevant literature. The methods are relevant, up-to-date, and clearly described. The results are interesting, novel, and many of them have been unexpected. The level of publications (joint first author) is high.

Still, a have a couple of comments. In the comparative gene expression analysis of iPSCs of the three studied species (page 69) clustering in addition to PCA would be desirable. In the same section, nothing is said about genes with decreased expression: is it due to the assumption that they reflect fibroblast specificity and hence are not interesting? — this needs at least to be discussed. Analysis of commonalities between human, mouse, and NMR DEGs ignores the fact that there are much less observed DEGs in mouse than in human and NMR. This requires an explanation (e.g. could that be due to differences in library sizes influencing statistical significance of fold differences?); anyhow, the number of DEGs should be accounting for when the overlaps in DEGs and GO categories / pathways in pairs are analyzed. A nice addition to Fig. 17 could be a panel with PCA for all species: would samples cluster first by species and then by cell type or vice versa?

On the technical side, the quality of some figures and tables is far from perfect. It looks like they have been copy-pasted from the papers in the pixel format, thus lowering the resolution instead of being reproduced / reformatted directly.

#### 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*