Skoltech

Skolkovo Institute of Science and Technology

# 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:**

| | |
|---|---|
| I confirm the absence of any conflict of interest<br><br>(Alternatively, Reviewer can formulate a possible conflict) | **Signature:**<br><br>**Date: 03-10-2018** |

*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

PhD thesis by Aleksei Mikhalchenko is a high level study in the field of cellular, developmental and molecular biology. The study is divided into 3 parts, connected by the same idea of studying the unique animal, *Heterocephalus glaber*, or the naked mole rat (NMR). This rodent is characterized by exceptional longevity, far beyond naturally expected for the terrestrial animal of its size. Moreover, NMR is known to naturally resistant to develop cancer and shown no increase in mortality with age. In addition, it is a social animal, with reproduction delegated to a "queen" of the colony. Yet another remarkable feature of NMR is that it is the only known poikilothermic mammal, that means it do not maintain constant body temperature. Due to the specificity in reproduction, normal way of genetic manipulations with NMR is highly complicated. This makes necessary to develop a method of production and manipulation with NMR induced pluripotent cells, which was successfully described in the part I of the thesis. The main result of this part is not only the production of iPSC, but also the production of mice-NMR chimeric animal, although with rather limited persistence of NMR cells. To compare it with other inter-rodent chimerae, the part II of the thesis goes about development of mice/rat chimera. An important conclusion about decrease of chimerism with the age of an animal was made. Finally, the III part of the work is devoted to the thorough study of the molecular mechanisms of NMR thermogenesis, which is remarkably different in its regulation with that of other rodents (and other mammals).

In sum, the study is done on he high level of the best international standards and I would recommend it for the *Thesis defense*

**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*