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Skolkovo Institute of Science and Technology

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Alexander Tyshkovskiy

PhD Program: Life Sciences

Title of Thesis:

MOLECULAR SIGNATURES AND MECHANISMS BEHIND LIFESPAN EXTENSION

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

I confirm the absence of any conflict of interest (Alternatively, Reviewer can formulate a possible conflict)	**Signature:** **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

The dissertation starts with the abstract that summarizes the main results obtained in this work. The results are clearly described and their significance for longevity research is clearly justified.

Chapter 1 is a review of the literature and it describes the data on aging and lifespan control, lifespan variation across the species with the main attention to naked mole rat (NMR) who unexpectedly long lifespan, lifespan variations among the species and the effect of different lifespan-extending interventions. The review is clearly written and I would recommend to publish it as a series of thematic review. At the end of this chapter author has placed a very important section that justifies the importance of the project that was a subject of the dissertation. Chapter 2 describes the approaches, results and discussion for the investigation of the effect of irradiation of the cells from NMR in comparison to mouse. Chapter 3 describes (similar to previous chapter) the mouse methylome signature in respond to aging and calorie restriction. Chapter 4 describes gene expression signatures in respond to different lifespan-extending interventions. Finally, Chapter 5 presents the major conclusions derived from the results of this work.

The topic of the research is of high general interest. Every person wants to live longer and be more health. There is huge amount of different studies all over the world and large number of the publications aiming to understand the mechanisms of aging and find the ways to extend the lifespan.

The work described in this dissertation provide a huge amount of information about the different cellular pathways used by long-living species, the pathways that differently activated in the normal animals and those with the extremely long lifespan in respond to DNA damage upon irradiation. More over the author has investigated methylome as the scale for aging and used it to investigate the influence of different substance known to extend the lifespan of various species on methylome signature. Thus, the author has suggested the system how to select the new compounds that may help in lifespan extension.

During his experiments the applicant used wide spectrum of modern techniques both experimental and bioinformatics that allowed him to use global approaches to investigate different signatures of aging for different species and in respond to different influences on the cells or organisms. The data are well presented, the results are well documented and the conclusions are well justified.

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 PNAS (IF 9.7) and as a second author in Aging Cell (IF7.6), one more paper is submitted.

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*