

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Dmitry Smirnov

PhD Program: Life Sciences

Title of Thesis: Investigation of the role of SIRT6 in the molecular mechanisms of the gene expression regulation, metabolism and aging

Supervisor: Assistant Professor Ekaterina Khrameeva,
Associate Professor Debra Toiber

Name of the Reviewer:

I confirm the absence of any conflict of interest

Assistant Professor Dmitry Ivankov

(Alternatively, Reviewer can formulate a possible conflict)

Date: 03-07-2023

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

In the presented PhD thesis “Investigation of the role of SIRT6 in the molecular mechanisms of the gene expression regulation, metabolism and aging”, Dmitry Smirnov investigated the role of the sirtoin6 protein in different biological processes in mammalian brain.

Three chapters of the PhD thesis devoted to the description of the results (Chapters 3, 4, and 5) comprise a core of the thesis. The other chapters contain Introduction (Chapter 1), Review of the Literature (Chapter 2) and Conclusion (Chapter 6).

In Chapter 3, Dmitry developed a pipeline of processing the lipidomics data coming from LC-MS method. I would like to stress that “Methods” section has a central position in this Chapter since it describes the organization of the pipeline. Taken into account common supporting role of a “Methods” section, it might be worth to entitle it as “Pipeline”, “Workflow” or similarly.

In Chapter 4, Dmitry established the link between deficiency of SIRT6 protein and decrease in expression of OXPHOS-related genes. Dmitry also demonstrated that deficiency of SIRT6 protein leads to abundance of TCA metabolites.

In Chapter 5, Dmitry found increased level of glioblastoma marker TP73-AS1 in the aging brain and under pathological conditions. Dmitry showed that SIRT6-related protein YY1 regulates TP73-AS1 level by activation the transcription of the corresponding gene upon TMZ treatment.

Overall, Dmitry developed a useful protocol for processing lipidomics data coming from LC-MS results, discovered important role of SIRT6 and YY1 proteins in gene expression and metabolism and showed intriguing similarity between aging and glioblastoma. The results of the presented works are scientifically significant and comply with the international level and current state of the art. The work is valuable for fundamental research. The publications are of high quality, the number of publications meets the requirements for the PhD thesis.

The thesis is written at a very good level of English. The thesis is formatted accurately; the number of typos is very low.

The dissertation conforms to international standards. It has a clear structure; the topic corresponds to the actual content.

To summarize, I rate the PhD thesis of Dmitry Smirnov as very interesting and important, of a high quality and scientifically significant.

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