

## Jury Member Report – Doctor of Philosophy thesis.

**Name of Candidate:** Smirnov Dmitrii

**PhD Program:** Life Sciences

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

**Supervisors:**

Assistant Professor Ekaterina Khrameeva, Skoltech

Associate Professor Deborah Toiber, Ben-Gurion University

**Name of the Reviewer:** Dr. Gabriel Leprivier, University Hospital Düsseldorf

I confirm the absence of any conflict of interest  (Alternatively, Reviewer can formulate a possible conflict)	<b>Date: 03-11-2023</b>
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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

The PhD thesis of Dmitrii Smirnov is well written and well organized. The introduction is concise, clear, to the point, giving the readers the exact information needed to understand the scientific context and what are the unanswered questions in the field. This naturally introduces and supports the biological relevance of the PhD projects, making the objectives of the thesis very clear. The work presented in this thesis is original, novel and of high scientific quality. The results are sound and the data fully support the conclusions drawn. The discussion parts and conclusion accurately depict the major findings of the thesis and place them in a broader perspective.

The data presented in this thesis fully answer the objectives of the PhD thesis and therefore the content of this thesis is highly relevant to the topic of the dissertation.

The experimental approaches consist of state-of-the-art technics. The methods used in this work are diverse and highly appropriate to address the biological questions. Furthermore, the candidate developed a data analysis protocol for lipidomics, which is a very challenging task that needs to be acknowledged.

The findings that the Sirtuin SIRT6 controls oxidative phosphorylation, mitochondrial activity, by selectively modulating the transcriptome in the brain, to restrict neurodegenerative diseases is of high scientific significance and represent an important contribution to our understanding of the molecular mechanisms of aging and of the role SIRT6 plays in this process. In addition, this work reveals that TP73-AS1, which is transcriptionally controlled by the SIRT6 interactor and transcription factor YY1, is overexpressed in aged brains as well as in glioblastoma. These further connect aging to glioblastoma tumorigenesis and further improve our understanding of the aging process. The results presented in this thesis fully comply with the international level and the current state of the art.

The PhD candidate published three articles, including two as first authors. Among those, one was published in the well-recognized journal Cell Death & Disease. This is a very good achievement for a PhD student in this field of research.

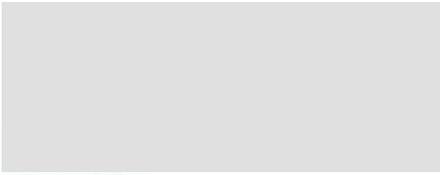
To me, this thesis is acceptable in its present form and does not require any changes.

#### **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*



Gabriel Leprivier, PhD