

## Jury Member Report – Doctor of Philosophy thesis.

**Name of Candidate:** Aleksei Mironov

**PhD Program:** Life Sciences

**Title of Thesis:** Tissue-specificity and regulation of aberrant alternative splicing

**Supervisor:** Assistant Professor Dmitri Pervouchine

**Name of the Reviewer:** Oleg Gusev

I confirm the absence of any conflict of interest  (Alternatively, the Reviewer can formulate a possible conflict)	<b>Date: 02-09-2022</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

Dear Colleagues, I am pleased to review the thesis “ Tissue-specificity and regulation of aberrant alternative splicing” presented by Aleksei Mironov. The research addresses the systematic analysis of two classes of aberrant splicing (TASS and USEs) by comprehensive analysis of existing transcriptomics databases. I found the dissertation nicely structured with a well-written introduction, and comprehensively arranged chapters describing two splicing events, followed by Discussion and clear Conclusions sections. The title of the dissertation properly matches and well-represents its content. The applicant applied a well-balanced variety of bioinformatics approaches to systematically analyze the splicing events. The methodological approaches fit the aim of the study.

In my opinion, the dissertation represents a well-thought and elegantly implemented study, fully matching international standards in the field.

I would like to emphasize that the applicant not only conducted a large-scale bioinformatics survey in dynamic, tissue specificity, and regulatory interrelation of splicing events but also carefully described many examples with specific genes, linking the mRNA expression with potential gene functions and its biological impact. I myself was excited about data representing specific miSS dynamics in heart fibroblasts and heart cardiomyocytes.

At the same time, I believe the study’s results should be more open to “an end-user”. The applicant may consider introducing an original online resource so that data on alternative splicing will be easily accessed by the research community and used in future projects.

Another point is that while the applicant used ENCODE data, there was no attempt to link the activity of specific regulatory elements (enhancer usage, alternative promotes) with aberrant splicing events. Why?

The quality of publications matches the standards of an international PhD degree. The only question is why a part of the dissertation (unproductive splicing) is not published or (at least) submitted to a journal.

Taking together I am happy to recommend that the candidate should defend the thesis by means of a formal thesis defense

Oleg Gusev

#### **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*