

## Jury Member Report – Doctor of Philosophy thesis.

**Name of Candidate:** Marina Kalinina

**PhD Program:** Life Sciences

**Title of Thesis:** Long-range complementary interactions in human pre-mRNAs and their implications in splicing


**Supervisor:** Professor Olga Dontsova

**Co-supervisors:**

Assistant Professor Dmitri Pervouchine

Dr. Dmitry Skvortsov, Lomonosov Moscow State University

**Name of the Reviewer: Dr. Timofei Zatsepin**

 I confirm the absence of any conflict of interest	<b>Date: 15-11-2021</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

Marina Kalinina performed a diverse study of RNA splicing devoted to the regulation of alternative splicing by complex intramolecular RNA-RNA interactions in trans and by transcription elongation rates. The methods used in the study are reasonable and results confirm the conclusions of the study. RNA-RNA interactions are rare key splicing regulators, especially long-range ones. I am happy to see that Marina did both bioinformatic analysis and experiments *in vitro* – a rather rare combination for PhD thesis. Marina performed a very deep study of Ate1 splicing – using minigenes and antisense oligonucleotides and under slowdown of RNA polymerase II. The high level of the study makes the results undoubtful, but the question if this mechanism is rare or super rare still arises.

The PhD thesis is well written in a classic way, literature overview is comprehensive, solid and up to date. Publications in high-impact journals and presentations at international conferences fit all criteria of the Skoltech PhD program and confirm the high level of this study. Current results are incompatible with the launching of a startup.

Since pre-defense my major concerns were answered, so I have only minor comments.

Minor points:

- p.28 “There are already two drugs forSMN2splicing correction approved by U.S. FDA (antisense oligonucleotide nusinersen inDecember 2016 and small molecule risdiplam in August 2020)”. I suggest to add Zolgensma to the list of SMA therapy
- p.37 “physico-chemical methods” I would dissect them according to common practice – into physical and chemical

This research is novel, original and thesis fits the criteria for PhD thesis in Skoltech Life Science PhD program. PhD thesis is ready for defense.

#### **Provisional Recommendation**

**X** *I recommend that the candidate should defend the thesis by means of a formal thesis defense*