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Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Anna Fefilova

PhD Program: Life Sciences

Title of Thesis: Functional study of human and murine morrbid lncRNA *in vitro*

Supervisor: Associate Professor Timofei Zatsepin

Name of the Reviewer: Dmitri pervouchine

I confirm the absence of any conflict of interest	**Signature:**  **Date: DD-MM-YYYY**

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

PhD Jury Member report

The thesis by **Anna Fefilova** entitled "Functional study of human and murine MORRBID long non-coding RNA in vitro" describes a functional study of the human lncRNA hMorrbid and its murine ortholog. The author has shown that the deletion of human Morrbid and CYTOR lncRNAs did not activate mitochondrial apoptosis pathway, but overexpression recovery of the M-217 transcript led liver cells to apoptosis. It is also reported that the murine ortholog of Morrbid regulates unproductive splicing of the proto-oncogene NRAS, presumably by interaction with SFPQ-NONO splicing complex.

The manuscript consists of Abstract, List of publications by the author, Introduction, Literature Review, Materials and Methods, Results, which is split as human (Chaper 4) and murine (Chapter 5), Discussion, Conclusions, Bibliography, and Supplementary material. Overall the dissertation is written in a clear and concise manner. I have some minor grammatical remarks such as missing or misused articles (e.g. "observed delay" => "observed a delay " on p.4), mixing past and present tenses, and the use of punctuation. However, there is no need to correct it. The Results section is clearly structured and contains all necessary statistical detail. In the Discussion section, the author goes over the results and discusses the question of whether Morrbid gene orthologs in mouse and human are functional homologs, which remains open.

My major and, in fact, the only concern is that the dissertation presents quite different results for two orthologous lncRNAs, human and mouse Morbid. As a potential reader, I would be interested to know how transferable are the findings on the regulation of murine NRAS splicing to its human ortholog and what implications it might have. The author doesn't discuss this matter until section 6.4, where the author says that "In human, no evidence for AS differential changes was found and the human NRAS gene does not produce PTC forms". I think it would be great to elaborate on how unusual it is, e.g., to give examples of human and murine lncRNA genes with diverged functions or to state it as a separate and important conclusion that she has identified the first such case.

The author has fulfilled all publication and conference requirements and wrote an excellent thesis. I therefore conclude that **Anna Fefilova** deserves to be awarded a PhD degree and wish her great success in the future career.

Sincerely,

Dmitri D. Pervouchine, PhD

Assistant Professor Skolkovo Institute for Science and Technology

3 Nobel st., Skolkovo Innovation Centre,

Moscow, Russia 143025

+7 (495) 280.14.81 * 3925

d.pervouchine@skoltech.ru
www.skoltech.ru

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*