


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: Pavel Ivanov

<p>I confirm the absence of any conflict of interest</p> <p>(Alternatively, Reviewer can formulate a possible conflict)</p>	<p>Signature:</p>  <p>Date: 15-11-2020</p>
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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 choice of the topic for this dissertation is timely. Biology and pathobiology of non-coding RNAs is rapidly developing area with excellent therapeutic perspectives.

The quality of the thesis is very good. It is clear that PhD candidate has been exposed to multiple opportunities to learn a number of various techniques. The thesis is technically sound and there are no ethical points to consider. Conclusions are supported by the data. The title and abstract of the thesis are supported by the conclusions. Figures and tables are adequate, however there are a couple of minor points listed below. The language is mostly clear. The methods used are relevant and adequate for actual goals of the dissertation.

Introduction is comprehensive, extensive and interesting to read, and contains references to the primary literature. This is a huge plus. However, some parts need more addition and rewriting.

Materials and Methods section is described in details.

Results section: Mostly clearly written with only minor issues to be fixed.

Discussion: I would appreciate detailed discussion of different approaches for LOF studies of ncRNAs. It would be useful to add actual discussion on the limitations and benefits of specific approaches.

Minor points:

Intro: NMD is a “nonsense-mediated mRNA decay” (and not ‘nonsense-mediated decay’). I feel that this part should be explained in more details as it largely different from themes described in this thesis.

Results and Discussion: I would add more information here with specific focus on why UPF1 is chosen for KD experiments to study effects of mMorbid in the regulation of NRAs mRNA isoforms. Also, it is not clear about the actual efficiency of UPF1 protein depletion in these experiments.

It would be useful to hear why PhD candidate has chosen these or other cell lines as adequate models for such experiments. What are the alternative models that could be used in these studies?

Whenever microscopy studies are present, scale bars would be appreciated. Whenever western blotting is shown, the sizes or markers should be indicated.

Regarding Fig. 31: Description in the text should be more clear. E.g., on page 126 it should be stated where transcript versus protein levels are measured (it is certainly about qRT-PCR based mRNA measurements, yet it sounds that for BMF, BAX and BAK, the levels of proteins were measured)... It is also not clear to me why protein expression levels in WT, KO, M-217 and R-217 cells were not measured except for BCL-XL and MCL1.

Fig 32: It is difficult to judge the actual changes in the levels of BIM proteins. If possible, a more representative image of fig 32a could be shown.

Publications: The candidate has one first author and one middle author original publications. Also, she is an author in one review article relevant to the topic of the dissertation. I estimate them as good level suitable for PhD defense and comparable to other PhD candidates in Russian Federation. No objections here.

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