

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:

<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: 11-11-2020</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

Anna Fefilova's thesis investigates the role of Morrbid lncRNA orthologues in human and mouse cells, particularly in the context of cancer, through a variety of molecular and genomic techniques. Overall the study finds that Morrbid is a highly complex lncRNA locus, and this is accompanied by complex roles in promoting/opposing cell viability and other cancer hallmarks.

Overall the thesis is very well presented. The writing quality is particularly good, the Introduction is concise and excellent. I see the Candidate has an admirable grasp of the scientific literature. However some explanations of important parts of the work remained unclear to this reader, such as the mutations engineered in KO cells in Fig24.

The research work itself reflects the difficulty of studying lncRNAs. The results are somewhat contradictory and it is fair to say that a clear-cut "story" remains to emerge from the data. The thesis does well to describe and interpret the data, but much more work remains to definitively elucidate the biological and disease role of Morrbid.

The techniques employed here were generally state-of-the-art and professionally done. It is an impressive body of work for a PhD thesis, and the integration with transcriptomics and proteomics was smooth.

Overall, it is difficult to judge the scientific relevance of some of the results here. Again, this is at least partially a reflection of the challenges thrown up by Morrbid itself- including its complex splicing. Nevertheless, some aspects of the story do not apparently lead to useful outcomes. One example of this is the finding that Morrbid regulates "poison-exon" splicing in NRAS. Apparently, this has no effect on mature NRAS mRNA or protein, so one struggles to find the disease relevance here. Similarly, while Morrbid is an extremely complex locus, the choice to focus in on one single exon for deep study seems rather arbitrary (although admittedly, I don't have a better suggestion). Finally, the nature of the deletion in Morrbid cells was somewhat unclear to me – if a huge deletion between two chromosomal arms is occurring as implied in Figure 24, then there is the concern that observed phenotypes could result from other genomic elements in that region.

Notwithstanding these difficulties, the work presented resulted in a solid publication and makes an important contribution to knowledge of enigmatic lncRNAs.

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