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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:

I confirm the absence of any conflict of interest (Alternatively, Reviewer can formulate a possible conflict)	**Signature:**  **Date: 10-11-2020**

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

- Brief evaluation of the thesis quality and overall structure of the dissertation.
  Thesis has canonical structure, well written review of lncRNA function evaluation and previous work on the function of Morrbid lncRNA. It comprises of 41 figures, 7 tables and 203 pages including supplement. The evaluation of experiments is logical and presented in a good style of scientific publication
- The relevance of the topic of dissertation work to its actual content
  Completely relevant
- The relevance of the methods used in the dissertation
  The thesis benefits of a plethora of molecular biological methods including splicing analysis using ASO, co precipitation of RNA with protein targets, cell culture CRISPR CAS/9 knockouts and many more
- The scientific significance of the results obtained and their compliance with the international level and current state of the art
  The results are highly significant and were published in IJMS a journal with constantly growing impact factor (now 4.5). Previous investigation of a similar depth on MORRBID function were published in Nature, although 4 years earlier
- The relevance of the obtained results to applications (if applicable)
  Not applicable
- The quality of publications
  High standard publications in Interantional Journal of Moleclar Scoience (first author) and in Mo Ther Nucleic Acids , middle author in a very good company Bob Lnger, Den Anderson , V Koteliansky

The thesis is tour de force investigation of MORRBID ad human orthologue in cell culture. Th experiments are logical and allow experiment based conclusions of the effect of MORRBID on the regulation of of proto-oncogene NRAS mRNA splicing, including formation of the isoform with premature termination codone (PTC). Author used both gain of function and loss of function of MORRBID/CYTOR in hepatocyte cell lines and provide conclusive evidence on the functional roles of this lncRNA in hepatocytes including highly clinically significant oncogenes NRAS and KRAS.

In my opinion knockout strategy of lncRNAs deleting the prmoter region was risky, but appeared successful which was confirmed by expression analysis. The rescue experiment was essential for interpretation of further resuts.

The novel mechanistic finding of the thesis was demonstration of direct interaction of SFPQ protein with both lncRNA Morrbid and NRAS mRNA, while the NONO protein interacts with Morrbid lncRNA.

In my opinion Discussion section is relatively short and could benefit from more detailed analysis of the own data in comparison with the previous findings of the function of described lncRNA in other cell types, particualy in leucocytes

Provisional Recommendation

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

X☐ *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*