Skoltech
Skolkovo Institute of Science and Technology

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Evgeniia Shcherbinina

PhD Program: Life Sciences

Title of Thesis: Role of lncRNA LL35 in hepatocytes function

Supervisor: Dr. Timofei Zatsepin, Velocity Global Rus

Name of the Reviewer: Yury Popov, MD, PhD

I confirm the absence of any conflict of interest (Alternatively, Reviewer can formulate a possible conflict)	Signature: Date: 13-08-2022

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

This is a thesis of PhD candidate Evgeniia Shcherbinina which represents a strong body of work on important and cutting edge topic on lncRNA function, and is performed using state-of-the-art techniques and approaches at the high, internationally accepted level.

The dissertation is focused on functional characterization of LL35 lncRNA in mouse species and results are quite comprehensive, identifying number of key functions of this lncRNA, as well as its relevance to disease such as liver cancer. Multiple approaches are utilized to study its function in vitro and in vivo, which is a strength of this work resulting in complete, conclusive results. Of note, the negative results are described thoroughly as well and data are critically appraised, according to the highest standard of scholarly work.

Results represent the significant advance in scientific knowledge and have important implications to the field of lncRNA, hepatology, as well as potential immediate therapeutic and diagnostic applications.

Evgeniia's publications are high quality and the productivity is appropriate to the level of training and stage of academic career.

I recommend the thesis to public defense, after addressing minor issues listed below. These are not critical and do not detract from the quality of work, but rather will allow to refine the data presentation and interpretation.

Specific comments:

1. Section 3.8 the principle of qRT-PCR (TaqMan?) should be specified
2. All legends to the figures should specify the number of biological replicates studied/used to build the graphs and calculate p value. Statistical tests and p value nature should be specified as well.
3. Fig. 28. ALT/AST and other LFTs units should be checked against the normal ranges, possibly assay calculation error
4. Since the hexokinase seems regulated by LL35, please briefly comment on possible involvement in dietary fructose metabolism, the question highly relevant to public health and liver disease
5. Important: interpretation of data in 4.7 should be refined to be more specific to what was studied – cell proliferation appears to be referred to interchangeably with that of cell survival. This needs to be critically revised.
6. Discussion may benefit from brief specific paragraph elaborating potential implications of results – for future research, therapeutic and diagnostic applications, specific diseases, etc.

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*