

## Jury Member Report – Doctor of Philosophy thesis.

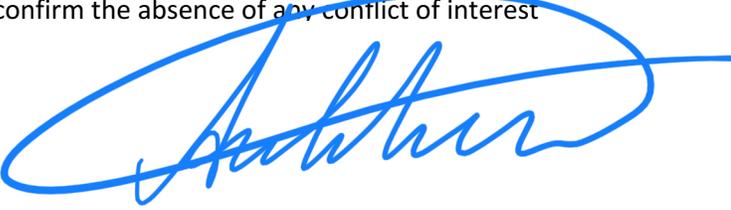
**Name of Candidate:** Mikhail Moldovan

**PhD Program:** Life Sciences

**Title of Thesis:** Heritable modifications of transmitted biological information as possible sources of adaptation

**Supervisor:** Professor Mikhail Gelfand

**Name of the Reviewer:** Yury Aulchenko

I confirm the absence of any conflict of interest 	<b>Date:</b> 04-08-2022
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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

*Brief evaluation of the thesis quality and overall structure of the dissertation*

The thesis is divided into six chapters. The thesis opens with a chapter providing a short introduction, followed by literature review, three chapters reporting results obtained by the aspirant. The remainder of the thesis offers a chapter on conclusions, a list of bibliography and supplements. The three chapters with main results each follow the classical structure of a scientific manuscript, with topic-specific introduction, methods, results, and discussion. With some exceptions, the structure of the dissertation is standard, clear, and easy to follow. Overall, the thesis is interesting to read and leaves very good impression.

*The relevance of the topic of dissertation work to its actual content*

The dissertation explores the topic of RNA editing and post-translational modification (PTM) from a new, evolutionary, perspective. Starting with an argument that mRNA-editing and PTMs are context dependent, with context being heritable, the author postulates that manifestation of these processes results in complex traits that may be subject to evolution. In the thesis, this postulate is explored. The author explores the data on mRNA editing sites in soft-bodied coleoid cephalopods to identify three types of editing site clusters that contribute to the transcript diversity and shows that A-to-I editing sites may enhance adaptation. The author then applies conceptually similar approach to one of well-studied PTMs, phosphorylation. The author developed a model for identification of phospho-islands and demonstrates that they are more conserved and are likely more adaptive than individual phospho-sites.

*The relevance of the methods used in the dissertation*

With reservation that the area of the thesis is not my direct expertise area, I found the methods used to answer the questions posed relevant and appropriate.

*The scientific significance of the results obtained and their compliance with the international level and current state of the art*

The results obtained in the thesis are significant and competitive at international level.

*The relevance of the obtained results to applications (if applicable)*

The study is of fundamental character, and I do not see any immediate practical applications. Fundamentally, the study does contribute to the broad understanding of genetics and mechanisms of evolution.

*The quality of publications*

The research performed in this thesis was reported in three peer reviewed manuscripts published in PeerJ and Scientific Reports. The publications follow high standard.

*The summary of issues to be addressed before/during the thesis defense*

- I would recommend formulating the aim and objectives of the thesis explicitly;
- In the introduction, at the end of section 1.1, the question is posed about “*the optimal rate of production of novel variants*”. This question is not really addressed by the research performed and the results obtained;
- Sorry for perhaps nitpicking, but I find the statement “*evolution may be regarded as the loop of information with two steps: i. Genotype that is decoded and phenotype is produced, ii. Mutation, selection and drift influence the frequencies of phenotypes and hence alleles underlying the*

*phenotypic values and the system returns to step (i).*” somewhat incorrect. In the context, in (ii) it is only the selection that affects phenotypes, while drift and mutation affect genotypes;

- It seems that you sometimes equate the transcriptome and proteome variability (e.g. the statement 3, “*Clustered editing contributes almost a half to the total transcript and proteome variability generated by editing*”). In general, the changes observed on the transcriptome level are far from being guaranteed to be passed to the proteome level. I would recommend that you avoid, or experimentally substantiate, this claim;
- I think some word(s) are either excessive or missing in the statement 5, “*Clustered phosphosites have more acidic contexts and are substituted to negatively charged amino acids than individual ones*”;
- For the sake of reader, the bibliography could have been formatted better by, e.g. having different indentation of the first and the next lines of each reference.

#### 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*