

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: Dr. Eugene V Koonin

I confirm the absence of any conflict of interest

Date: 04-08-2022

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

Mr Moldovan's dissertation addresses a question of major interest and fundamental significance, the contribution of non-genetic changes, such as RNA editing or protein phosphorylation, to genetic variability. The dissertation explores the connections between these RNA and protein modifications and hereditary genomic mutations in two systems, coleoid cephalopods, which are known for unusually extensive RNA editing, and mammals, where proteins are abundantly phosphorylated. For both systems, Mr. Moldovan and colleagues show that the modification sites in both RNA and proteins are specifically prone to the corresponding genetic changes: A to G mutations in the case of RNA editing and mutations to negatively charged amino acids in the case of protein phosphorylation sites. These are important, novel findings demonstrating evolutionary synergy between genetic and non-genetic changes to information carriers in living organisms.

The dissertation is exceptionally thoroughly researched, well organized and clearly written. The versatile bioinformatic methods used in this work are all state of the art and have been applied appropriate and moreover with exceptional care. The entire study conforms with the highest international research standards. The applicant has three publications in high quality international journals. The work of Mr. Moldovan open new research directions and poses important questions on the exact mechanisms of the observed phenomena, but pursuing these directions is certainly beyond the scope of the dissertation. To conclude, this is an excellent dissertation that needs no modification before the defense.

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