

## Jury Member Report – Doctor of Philosophy thesis.

**Name of Candidate:** Vita Stepanova


**PhD Program:** Life Sciences

**Title of Thesis:** Metabolic variations of modern and ancient human populations

**Supervisor:** Prof. Philipp Khaitovich

**Date of Thesis Defense:** 19 December 2019

**Name of the Reviewer:** Dmitry Ivankov

I confirm the absence of any conflict of interest  (Alternatively, Reviewer can formulate a possible conflict)	<b>Signature:</b>   10-12-2019 <b>Date: DD-MM-YYYY</b>
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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

In the presented PhD thesis "Metabolic variations of modern and ancient human populations" Vita Stepanova analyzed differences in metabolome and lipidome among different organism groups.

First, Vita analyzed differences in lipid and metabolite compositions of prefrontal cortex among modern human populations and showed that Han Chinese differ from West Europeans and African Americans, which are relatively close to each other. Second, she compared the metabolomes of different organs among humans, chimpanzees and macaques. Vita found that metabolites related to oxidative phosphorylation and purine biosynthesis in human brain are underrepresented comparing with those from apes. Utilizing transgenic mice and human cell lines, Vita Stepanova experimentally demonstrated that gene coding for adenylosuccinate lyase is responsible for the observed difference. Vita also identified the mutation responsible for the observed behavior. The presented discoveries are principally new and open opportunities to study metabolome and lipidome using transgenic mice and cell cultures.

The results of the presented work are scientifically significant and comply with the international level and current state of the art. The work is perspective for future applications and fundamental research. The quality of the publications is high, and the number of publications suits the requirements for the PhD thesis.

The dissertation conforms to high international standards, it has a clear structure, the topic corresponds to the actual content.

The number of misspellings in the thesis is low. Though, there is a principal one: at page 29 Vita writes "(hypergeometric test,  $p = 3.5e^{-54}$ )". Probably, she copy-pasted the results of the test and did not correct the p-value to be equal to  $3.5 \times 10^{-54}$ . The other typo is presented in the content where the automatic markdown procedure did not find the list of the figures and wrote in Russian "ОШИБКА! ЗАКЛАДКА НЕ ОПРЕДЕЛЕНА.". The other typos are tolerable, the annotated pdf file was sent to Vita. Overall, the typos do not influence the overall good impression from the thesis.

To summarize, I rate the PhD thesis of Vita Stepanova as very important, of high quality and scientifically significant.

#### 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*