

Jury Member Report – Doctor of Philosophy thesis.


Name of Candidate: Aleksandra Mitina

PhD Program: Life Sciences

Title of Thesis: Role of breast milk lipid composition in postnatal brain development

Supervisor: Professor Philipp Khaitovich

Name of the Reviewer:

<p>I confirm the absence of any conflict of interest</p> <p>(Alternatively, Reviewer can formulate a possible conflict)</p>	<p>Signature:</p>  <p>Date: 07-11-2020</p>
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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

The dissertation devoted to the mass-spectrometry analysis of milk and brains in several species. The text has a typical structure. It starts with an abstract, publication list, Acknowledgements. The main text contains standard chapters – Introduction, Material and methods, Results, Discussion.

The first chapter, Introduction, contains a review. The review provides basic information on current research related to the topic of the dissertation, namely the evolution of lactation, the role of lipids in brain development, mass-spectrometry of lipids. The review contains about 100 references.

Chapter Material and methods describe the preparation of the biological samples of milk and brains. The milk samples were taken from humans, macaques, pigs, cows, goats, and yaks. The human and cow samples were taken from two locations – Moscow and Shanghai. The brain samples were taken from humans, chimpanzees, macaques, goats, pigs.

The central chapter, Results, describes the research. All the samples were analyzed by Mass-spectrometry and its lipid content was obtained. The analysis of the samples shows the species specificity of the lipid content. The most interesting result is the correlation between the lipid composition of milk and the brain. The main driver for this correlation is long fatty acids.

The last chapter, Discussion, summarizes the research.

The results of the research are well published in two papers in good journals – BMC Evol Biol (impact factor 3.05) and Proc Natl Acad Sci U S A (impact factor 9.41).

Nevertheless, I have some comments and questions.

1. p.12. “Mature lactocytes produce lactose, a unique oligosaccharide found only in milk” – lactose is a disaccharide.
2. P.12 “ lactose draws much water under osmotic pressure, diluting milk and thus lowering concentrations of fat and protein” – if lactose binds water the concentration of fat and protein should increase.
3. p.33 “cows (n= 4)” Domestic cows are a product of selection, including for the fat content of milk. Were the cows of the same breed or different, were the cows of the same age?
4. Fig 1 – Milk lipidome evolution – incorrect figure title. Evolution is a time process while the figure presents only phylogenetic relation. Panel C – the color notation should be described.
5. p.35 What is residual variance in MDS (fig.1B)?
6. p.43 PCA (Figures 5,6) shows a significant difference between Moscow and Shanghai populations. Is this difference due to the race difference or nutrition?

7. p.53 Clustering on Fig.12A is not obvious.
8. p.67 I can not understand: “This analysis demonstrated that linoleic (18:2), alpha-linolenic (18:3), docosahexaenoic (22:6) and tetracosapentaenoic (24:5) FAs were present at significantly higher levels in human breast milk”, but in figure 17 these FA show log fold change about 0, while 28:1, 28:2, 26:1, 27:1 really have a significant fold change in the brain (PFC as well as CB). Moreover, only these FAs define the correlation – without these points, the correlation coefficient became near zero.
9. fig.18A – the confidence intervals should be shown

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