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Skolkovo Institute of Science and Technology

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: Maria do Rosário G R Marques Domingues

I confirm the absence of any conflict of interest	**Signature:**  **Date: 11-11-2020**

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 thesis titled "ROLE OF BREAST MILK LIPID COMPOSITION IN POSTNATAL BRAIN DEVELOPMENT, submitted by Miss. Aleksandra Mitina, makes a significant contribution in the study of milk composition across animal species, and also to unravel the possible relationship between breast milk lipid composition, a major source of essential fatty acids, with brain lipidome , and to find define human-specific lipids .

The Ph.D. thesis is original, addressing an important topic from a scientific point of view, using state of the art technology of liquid chromatography mass spectrometry based lipidomics, and presenting innovative results.

The thesis is very well organized and very well written. The literature cited supports, with consistency, the introduction, the work developed and the discussion of the results presented. The scientific work developed in this thesis is of very high quality, and is validated by the number of publications in international journals with high impact factor. The results obtained were presented to the international scientific community in two published papers.

The thesis is well written, very well organized. It starts with an abstract, followed by an introduction section including major scientific question to adress, results and discussion and bibliography.

Introduction section presented a good review of the literature on the subject area, highlighting the state of the art concerning the main interest and biological relevance of lactation in mammals and in the evolutionary point of view. In this section it is also addressed the composition of milk and the relevance of lipids as main nutrient, and making special attention of its importance as a source of essential fatty acids for brain development. It would benefit this chapter, namely in section 1.2, if have been added a brief description of the composition of lipid profile (phospholipid and other polar lipids where FA are esterified) of brain in more detail, to complement the very nice description of fatty acid composition. The state of the art technological approaches to study lipids in biological samples are also described.

The methods are very clear and appropriate. In this work advanced liquid chromatography coupled to mass spectrometry approaches using different instruments, selected as being more adequate for the analysis of fatty acids and lipidome were used evidencing the high technological

level of this work. The number and diversity of samples analysed is impressive. It would benefit this chapter to detail the methods used in the statistical analysis done for the exploitation of the data.

Results are presented in four chapters. The chapters 3.1 and 3.2 present new findings in the identification of the lipid composition in breast milk after analysis comparing several mammals and including samples from healthy humans from two different populations, respectively comparing the lipid composition(in capter3.1) and fatty acid composition obtained after hydrolysis(chapter 3.2). The third chapter describes the comparison of lipid composition of the fatty acid in distinct brain regions, and in different mammal's species. In the last chapter of the results section, and integrate comparison of lipid composition of brain and breast milk is done to pinpoint the contribution of maternal feeding and milk composition with brain development, in each mammal species. This this section would benefit if the list of identified lipid species had been included, for example in the annex.

The last chapter, the discussion, the relevance of the results are addressed, showing how it relates to the literature and research questions, to support the overall conclusion. The literature cited supports, with consistency, the introduction, and discussion of the results.

The results obtained in this work were published in scientific paper in per reviewed journals with high impact factor supporting the scientific quality of the work.

I can clearly declare that this thesis is a significant contribution to field of breast milk and brain lipidomics and their biological relevance. It is a Ph.D. thesis with a very high quality. There are some minor points of detail that the candidate could improve, but this is not going to affect my overall positive judgement. I think that the thesis makes a significant original contribution.

Hence, I give a very high recommendation for this thesis and I strongly recommend the thesis for the public defense on December 11.

Provisional Recommendation

X *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*