

## Jury Member Report – Doctor of Philosophy thesis.

**Name of Candidate:** Ilia Kurochkin

**PhD Program:** Life Sciences

**Title of Thesis:** Comparative analysis of human brain based on mass-spectrometry data

**Supervisor:** Prof. Philipp Khaitovich

**Chair of PhD defense Jury:** Prof. Mikhail Gelfand

**Email:** [m.gelfand@skoltech.ru](mailto:m.gelfand@skoltech.ru)

**Date of Thesis Defense:** 26 October 2018

**Name of the Reviewer:**

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|---|---|
| <p>I confirm the absence of any conflict of interest</p> <p>(Alternatively, Reviewer can formulate a possible conflict)</p> | <p><b>Signature:</b></p>  <p><b>Date: 14-10-2018</b></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**

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

This is a cohesive work devoted to metabolome and lipidome of the human brain. A comparative approach is used throughout; for comparison, human vs. non-human species, disease phenotypes, and other tissues are used. The main text includes three chapters, which are laconic but comprehensive.

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

The title matches the content well.

- **The relevance of the methods used in the dissertation**

Large datasets are analyzed, which allows to pick up minor effects. I am not a specialist in mass-spectrometry, but all the wet lab work and low-level analysis seems solid. I want to stress particularly the solidity, clarity and rigor of the statistical analyses (and the high quality of the figures).

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

Front edge stuff.

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

The obtained results may be of relevance for drug design, and (when overlapped with genetic data) can be used to better understand the genetics and physiology of these diseases.

- **The quality of publications**

High, in high-level journals in the field.

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

The thesis is very well written and illustrated, and the results are well supported by the data. I have only a few comments concerning presentation or interpretation.

The literature review covers much of the relevant literature. It would be interesting to also consider here the genetic determination of the metabolites/lipids level, e.g. in enzymes catalyzing reactions associated with them. Such results are mentioned in the text (e.g. p. 38); is there no prior literature on this?

The finding that only a tiny fraction of lipids evolves in a clock-wise fashion is very interesting; however, I do not see the ground to reject immediately the "neutral" explanation for this evolution as done by the author. Perhaps the rest of the lipidome is functional, and much of its divergence is also functionally relevant, and therefore strong. Even for genomic data, there are case out there when just a very small fraction of the genome evolves neutrally, with the rest being functional (e.g., in *Drosophila*, just short sequences at the middles of introns are considered functional).

At the bottom of p. 44, I am confused. Are the overrepresented changes in module 4 in the same direction in ASD as in human as a species? This looks interesting, but unclear.

#### **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*