

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

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Date of Thesis Defense: 26 October 2018

Name of the Reviewer: Christoph W. Turck

<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: 25-09-2018</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

Appraisal of Mr. Iliia Kurochkin's Ph.D. thesis entitled:

Comparative Analysis of Human Brain Based on Mass Spectrometry Data

Mr. Iliia Kurochkin's Ph.D. thesis is an important contribution to the elucidation of molecular mechanisms involved in neurocognitive disorders including Autism Spectrum Disorders (ASD) and Schizophrenia (SZ). For this purpose Iliia has compared prefrontal cortex tissue from diseased patients and healthy controls using lipidomics and metabolomics analyses. Several of the identified changes between disease and control are lipids and metabolites that are human-specific. Some have been previously found in peripheral body fluids from ASD and SZ patients.

Iliia has further extended his project with an analysis of the lipidome in 6 tissues from 32 species. He was able to show that many of the human-specific lipid features are part of molecular pathways affected in ASD and SZ. This led him to conclude that the evolution of cognitive abilities in higher species is reflected in brain lipid and metabolite profiles.

Iliia's thesis project, the large-scale lipid and metabolite profiling analyses of prefrontal cortex tissue from many species, is the first of its kind. The fact that a significant number of the identified lipid and metabolite changes in ASD and SZ are also present in peripheral body fluids is not only of value for basic neuroscience research, but has also potential for applications in the field of medical diagnostics.

Overall the thesis is extremely well written, logical, critical and very detailed covering every aspect of the project. In the 'Introduction' Iliia provides an overview and background of ASD and SZ including genetic findings. He points out that the effect of genetic variants is very small and so far has not provided much insight into the etiology of ASD and SZ. The lipidome and metabolome data Iliia has acquired are arguably a much closer representation of the phenotype than the genetic data. In this regard, the comprehensive lipidome and metabolome analyses have allowed Iliia to delineate molecular pathways implicated in ASD and SZ etiology. This is an important contribution and will enable future studies aimed at further investigating the mechanism of these disorders. In addition, the identified lipid and metabolite level differences represent much sought after AD and SCZ biomarker candidates that are critical for diagnostic applications. Especially the ones that are also present in peripheral body fluids can serve this purpose.

The mass spectrometry technologies used for lipidome and metabolome data acquisition as well as data analysis methods including statistics and machine learning that Iliia employed in his project are all state of the art and explained in great detail in his thesis. The results are clearly presented including all methods that were used with a thorough assessment of their relevance and caveats. Also impressive is the breadth of methods that were used.

Iliia provides an extensive review of the literature for ASD, SZ and previously carried out lipidomics and metabolomics studies for these disorders. He also elaborates on the technology he is employing in his project. All of this is backed up with a list of relevant references.

Iliia is a co-author on two high impact publications and first author on a manuscript in preparation about the results of his thesis project.

In summary, Ilia has demonstrated in his dissertation his ability to work independently as well as a team member with experts in the methods that were needed for his studies. He is able to interpret results in a critical manner and provides suggestions for future experiments.

I recommend that the thesis be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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

Some discussion on the possible applications of the identified lipid and metabolite information would be appropriate. Better patient group stratification tools are in great demand in psychiatry! Specific molecular markers detectable in the periphery would revolutionize current diagnostic procedures that are mainly based on imprecise rating scales.

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