

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Kseniia Safina

PhD Program: Life Sciences

Title of Thesis: Molecular epidemiology of socially important infectious diseases

Supervisor: Professor Georgii Bazykin

Name of the Reviewer: David van de Vijver, PharmD PhD, associate professor

I confirm the absence of any conflict of interest

(Alternatively, Reviewer can formulate a possible conflict)

Date: 10-11-2021

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

I have read the PhD thesis of Kseniia Safina with great interest. Ms Safina reports on the use of molecular epidemiology for studying HIV and SARS-CoV2 in Russia. In the first chapters Ms Safina lays the theoretical basis for the remaining part of her thesis. She starts with providing a background on molecular epidemiology, then continues to provide the scientific basis of HIV and SARS-CoV2. In chapter 3, the analysis of the HIV epidemic in Oryol are described which is followed by a study on SARS-CoV-2. The analysis that are described have been performed in a very thorough way and are of great scientific quality. The work on SARS-CoV-2 has been published in Nature Communications which is one of the best scientific journals in the World. In the following paragraphs, I will outline my comments on the thesis, report on the quality and mention three topics that should be modified before the defense.

Brief evaluation of the thesis quality and overall structure

The quality of the thesis is high. Ms Safina shows that she has a thorough understanding of not only molecular epidemiology but also of important virological aspects that explain phylogenetic analysis. A good example of her knowledge of virology is the section in which she described bottleneck events in HIV transmission and how this is affecting within host evolution (section 2.2.2). The thesis has resulted in a publication in a high impact journal which is also indicative of the high quality of the work.

The thesis has a good structure. Ms Safina starts with explaining the background of molecular epidemiology and then continues with a background on HIV and SARS-CoV-2. What in my view is missing, is a more thorough discussion of the implications of the work that was included in the thesis. In its present form the conclusion summarizes what has been found without mentioning the implications or recommendations for future pandemics. At the end of my report, I will suggest what I believe should be added to the thesis before the defense. Having said this, my view of the thesis is and remains very positive.

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

Ms Safina has addressed a very relevant topic in her dissertation. As Ms Safina outlines in her work, molecular epidemiology is important to understand how viruses are spreading across geographical regions. This is a very important topic as the current COVID pandemic is showing. The aims that are outlined in the beginning of the thesis have been addressed and as such the dissertation matches the content.

The relevance of the methods used in the dissertation

The thesis includes all relevant methods that are used in phylogenetic analysis. The analysis that are included have been performed in a very thorough fashion and are relevant for the research aims that are addressed.

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

The results have a strong scientific significance as has also been shown by the fact the study on SARS-CoV2 is published in Nature Communications. What I am missing is a discussion on how the results of the thesis could be used in containing HIV and SARS-CoV2. As such, the thesis has a strong emphasis on the technical aspects of molecular epidemiology, which is fine, but I would like to see a discussion on the implications.

The quality of publications

As written before: having a paper in Nature Communications is impressive. I am sure that the work on HIV in Oryol also will be published in a good journal.

Recommendations

As can be read, my overall impression of the thesis is high. Nonetheless, I believe that at some points the thesis can be improved. I therefore make the following three recommendations, that I would like to have changed before the defense:

1. *Section 2.1.2 on modern molecular epidemiology*

Although, the theoretical background in the thesis is of a very high quality, I found section 2.1.2 a bit difficult to follow. In this section a lot of modern concepts are not very well described. For instance, the part on the Ebola outbreak of 2014-16 only lists what insights molecular epidemiology provided without giving further details. In my view, this section can also be improved by using sub-headings.

2. *Page 36 on HIV transmission in the United Kingdom*

It is mentioned that there is a higher risk of MSM transmission. This suggest that risk of HIV transmission among MSM is increasing over time, which is not the case (the number of new infections among British MSM is declining). In the next sentence it is also mentioned that there is a growing role of HIV transmission among MSM and IDU in the UK. This is not true, as HIV transmission in these groups is declining. The number of new HIV diagnosis among IDU in the UK is quite low.

3. *Discussion*

The discussion in its present form is quite brief. I would like to invite the candidate to elaborate a bit further on implications of her work for e.g. public health and for molecular epidemiology. The study in Oryol identifies transmission clusters. Could we use these clusters to reduce the size of the HIV epidemic and how? What are the implications of her work for future pandemics? Are there improvements needed in molecular epidemiology?

In summary, I believe that Ms Safina wrote an excellent thesis. If my recommendations are followed then I recommend that she can defend her thesis by means of a formal defense.

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