

## Jury Member Report – Doctor of Philosophy thesis.

**Name of Candidate:** Evgeniia Alekseeva

**PhD Program:** Life Sciences

**Title of Thesis:** Evolutionary analysis of intrahost interaction between pathogens and adaptive immunity

**Supervisor:** Professor Georgii Bazykin

**Name of the Reviewer:** Assistant Professor Ekaterina Khrameeva

I confirm the absence of any conflict of interest

(Alternatively, Reviewer can formulate a possible conflict)

**Date: 12-06-2023**

*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.**  
The thesis joins two studies. The first one examines how B cell immunity adapts to rapidly changing pathogens using affinity maturation of B cell clonal lineages. The second one studies a case of long-term COVID-19 in an immunocompromised host. Both studies are of excellent scientific quality, which is supported by publications in high-ranking journals.
- **The relevance of the topic of dissertation work to its actual content.**  
As both studies include evolutionary analysis of intrahost interaction between the adaptive immunity and the pathogen, the topic of the thesis is relevant to its actual content.
- **The relevance of the methods used in the dissertation.**  
Methods used in the thesis are relevant and applied correctly, to my best knowledge, in both presented studies. The used methods are well described and presented with enough details.
- **The scientific significance of the results obtained and their compliance with the international**

**level and current state of the art.**

Both works utilize evolutionary analysis of host-pathogen interaction and achieve excellent results, therefore demonstrating the power of this approach, which is a state-of-the-art method for studying adaptive immunity and dynamics of intrahost pathogen evolution. Thus, this thesis copes with the international level. Few studies consider the evolution of B cell clonal lineages from the phylogenetic point of view. Thus, the results described in the thesis are novel and interesting.

- **The relevance of the obtained results to applications (if applicable).**
- **The quality of publications.**  
High enough to pass the PhD program requirements.

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

The thesis of Evgeniia Alekseeva presents an excellent work, both in research content and in writing. It describes two studies on the evolutionary analysis of short-scale intrahost interaction between the adaptive immunity and the pathogen.

The literature review presents a detailed description of existing knowledge on adaptive immunity and evolutionary analysis of B cell clonal lineages and overviews previous studies of B cell clonal evolution. It is very well written and contains all the details necessary for understanding of the research presented in next chapters.

The literature review is followed by Chapter 3, which contains a slightly modified text of the paper (Mikelov et al. 2022). It looks a bit unusual to me that this chapter contains its own Introduction section. This Introduction section was apparently copy-pasted into the thesis from (Mikelov et al. 2022) with little modifications, which is ok, but it seems to be excessive because the thesis already has an Introduction section at the beginning and a detailed literature review. This additional Introduction section repeats what has already been described above.

The same comment goes to the Introduction section at the beginning of the Chapter 4. I would recommend replacing it with some text linking Chapters 3 and 4.

Regarding the presentation of the results, I have very few comments because the quality of the performed research is excellent.

- In Fig. 3.2G, it is not clear how the two-sided Mann-Whitney test was applied to calculate the statistical significance in this case. Fig. 3.2G presents two fractions while the Mann-Whitney test is applied to some distribution(s) of values. The procedure should be better described.
- In Fig. 4.1B, it is unclear what the legend Coverage Depth describes. It seems unrelated to the Fig. 4.1B. Probably, it is related to the Fig. 4.1D and should be moved there.
- Is it possible to calculate the statistical significance in Fig. 4.3B,D?

In the Conclusions chapter, the link between the two parts of the work should be better articulated. Ideally, this chapter should contain one list of conclusions (with clear links between them) instead of two separate lists. And I would recommend adding a small paragraph to the very end of this chapter, which would sum up both parts of the work. I.e., a more general concluding paragraph is missing here.

**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*