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# Jury Member Report – Doctor of Philosophy thesis.

**Name of Candidate:** Artem Mikelov

**PhD Program:** Life Sciences

**Title of Thesis:** Dynamics of immunoglobulin repertoires in memory and antibody-secreting B cell subsets in health and disease

**Supervisor:** Associate Professor Dmitriy Chudakov

**Name of the Reviewer: Ola Grimsholm, PhD, Medical University of Vienna**

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| I confirm the absence of any conflict of interest<br>Confirmed. | **Date: 23-03-2023** |

*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**

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

Report from Grimsholm, Ola PhD (Medical University of Vienna)

Brief evaluation of the thesis quality and overall structure of the dissertation

The PhD Thesis presented by doctoral candidate A. Mikelov is overall well written and covers the most important areas of B-cell biology related to his results. It covers the relevant references in an unbiased manner.

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

The introduction to the topic is relevant to the results presented and I believe they are enough in depth so no further text needs to be added. However, I believe it would benefit from more editing especially so that abbreviations are used in a consequent manner throughout the Thesis. Please also check the headlines again and their correspondent part in the Table of Contents, there are some mistakes. I also noticed a few places where minor changes would be necessary:

On p. 20-21 it is discussed about also GC-independent memory B cells and whether they can be somatically mutated or not. Recent data would argue that some amount of SHM can be achieved also in extrafollicular reactions (see for example excellent review by Shlomchik https://doi.org/10.1016/j.immuni.2020.11.006).

Later on the same page it is mentioned about the GC fates of B cells but apoptosis is not discussed. This is one of the main fates and needs to be mentioned.

The relevance of the methods used in the dissertation

The methods used for this Thesis are highly innovative and state of the art technologies for studying BCR repertoires. The Thesis also recognizes the weaknesses of e.g. using RNA vs. DNA for Ig sequencing, which is nicely discussed.

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

The results presented in this Thesis are of top international quality and published in leading journals such as eLife. The data is clearly presented and easy to follow. The demonstration of the stability of the memory repertoire over time is novel and very important for our understanding for how the immunological memory is preserved in individuals. It has important implications for vaccine development. The observation of a minor public repertoire of memory B cells with lower amount of SHM as compared to the private clonotypes is very interesting and would as suggested in the Thesis argue for a common repertoire against certain pathogens that could be possibly present already in the germline repertoire.

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

The tool (MiStrainer) developed in this Thesis have many applications in the AIRR field. It makes it easier for other groups to explore this field of new Ig alleles since the amount of data needed is more limited than in other existing tools like IgDiscover and the comparison in the Thesis with TigGER shows that MiStrainer is more efficient in detecting allele variants.

The quality of publications

2 out of 3 publications are published in highly reputable international journals where the publication in eLife is a top notch paper with important implications for the front of the B-cell research field.

| **Provisional Recommendation** |
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| ☒ *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* |