

Jury Member Report – Doctor of Philosophy thesis.


Name of Candidate: Sofya Kasatskaya

PhD Program: Life Sciences

Title of Thesis: Origin of T cell subsets studied through the lens of TCR repertoires

Supervisor: Associate Professor Dmitriy Chudakov

Name of the Reviewer:

I confirm the absence of any conflict of interest (Alternatively, Reviewer can formulate a possible conflict)	Signature: Asaf Madi  Date: 24-05-2021
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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

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



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Re: PhD thesis evaluation report

Dear colleagues,

It was my pleasure reading the PhD thesis, entitled: "Origin of T cell subsets studied through the lens of TCR repertoires" and I appreciate the artwork by David Goodsell on the cover. This PhD thesis submitted by Sofya Kasatskaya has concluded in two first author and four co-authored publications in the field in journals such as *eLife*, *Front Immunol.* and *Nature Immunol.* which is an infrequent accomplishment for a PhD student. Sofya worked on few different projects that were all revolved around the research of T cell receptor repertoires, which is a relatively new field in immunology. Like most developing fields the community will keep improving and adjusting ways to obtain and interpret the data as technology progress but yet being one of the first to tackle these problems is a big achievement making her one of the experts in the field.

In her research Sofya first looked at the peripheral selection, survival, and aging of human naive T cells, comparing young and aged donors finding that that age-related changes in TCR repertoires include shortened and less diverse CDR3 regions of TCRs. Secondly, she continued to look at the selection and survival of naive T cells in the fetal gut where she and her colleagues found evidence of memory in helper T cells acquired in embryonic intestinal tissue. She then investigated sorted Th1/Th2 and Th17/Treg subsets from healthy donors and provided a detailed picture of distinct repertoire features, plasticity, and publicity of helper CD4 T cell subsets. She also looked at the role of TCR structure in the biology of human gamma/delta T cells in peripheral blood and extended her research also to tissues. Importantly she adapted the TCRbeta sequencing protocol created earlier in our laboratory to the needs of TCR delta chain sequencing. Finally, she used these tools to study the role of public T cell receptors in cancer surveillance on an example of gamma/delta TILs in breast cancer samples.

Together, this thesis contributes to a more comprehensive model of the TCR repertoire landscape and its changes across functional T cell subsets, across locations of systemic and tissue-specific immunity, and across the human lifespan.

While the different methodologies used throughout the thesis are complicated the thesis is well written, clear and easy to follow. Importantly, the figures are in high quality and self-explanatory as is expected from a work that summarizes published articles. The conclusion paragraph at the end of the thesis is satisfactory in terms of limitations and future directions but lacks some meta-analysis interpretation. Thus overall the submitted thesis meets the general requirements for this type of academic works.

I would ask Sofya to add both a paragraph that gives the reader some meta interpretation, a conclusion she can draw from her vast experience as well as, a short paragraph describing the ethical implications of her work specifically but not limited to the immune-aging.

The combined work presented in this thesis is original and expected to significantly advance the understanding in the field. Therefore I gladly recommend the acceptance of this thesis, by the candidate Sofya Kasatskaya, as a partial fulfillment of the requirements for the degree of Doctor of Philosophy.

Best regards,

Asaf Madi, PhD

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

