

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Dmitry Sutormin

PhD Program: Life Sciences

Title of Thesis: Regulation of bacterial genome topology by topoisomerases

Supervisor: Professor Konstantin Severinov

Name of the Reviewer: Konstantin Lukyanov

I confirm the absence of any conflict of interest	
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	Date: 11-08-2022
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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

Topoisomerases are ubiquitous enzymes that relax DNA supercoils, which inevitably appears during replication, transcription, recombination and genome condensation. Their action is indispensable for both pro- and eukaryotic cells. In spite of decades of research, many important features of topoisomerase functioning in live cells remain unclear. Besides obvious fundamental interest, topoisomerases possess high medical significance since they are promising targets for antibacterial and anticancer therapies.

In the present work, Dmitry Sutormin with colleagues developed a novel method, Topo-Seq, that enables precise genome mapping of a target topoisomerase with a single nucleotide resolution. Development of Topo-Seq is a significant methodological advance, which undoubtedly will be used in many laboratories all over the world. Notably, according to Scopus, there are already 21 citations of the Dmitry's NAR 2019 paper on the Topo-Seq method.

With a novel method in hands, Dmitry studied *E. coli* genome-wide distribution of three topoisomerases, namely, DNA gyrase, Topo IV, and Topo I. Their binding motifs were deciphered, and accumulation at different parts of genes was demonstrated. Moreover, functional association with transcription and replication was revealed.

The main results of the dissertation were published in Nucleic Acids Research (IF 19.2) and Nature Communications (IF 17.7), both papers with the first authorship of Dmitry Sutormin. A comprehensive review on topoisomerases was published in Acta Naturae (IF 2.1). Additional paper with Dmitry as a corresponding (last) author appeared in Life (IF 3.3).

Overall, this is a top-quality work. I have couple of formatting-related comments only:

Pages 37, 50: Some words are in red, probably left over from a draft.

Fig. 26: Designations on the panel D are invisible (too small). Also, designations on the panel F are quite small.

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