

Jury Member Report – Doctor of Philosophy thesis.


Name of Candidate: Anna Shiriaeva

PhD Program: Life Sciences

Title of Thesis: Interference and primed adaptation intermediates in type I CRISPR-Cas systems

Supervisor: Professor Konstantin Severinov, Skoltech

Name of the Reviewer:

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| I confirm the absence of any conflict of interest (Alternatively, Reviewer can formulate a possible conflict) | Signature:  Date: 09-10-2020 |
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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 thesis has canonical structure, well written and contains 170 pages, 35 figures, of which 24 are in the Results section presenting original experiments of the author. The review sets the prior art knowledge in the field and sets the goals and aims of the dissertation. The results are well presented, the discussion is concise and relevant to the experimental data. Conclusions are sound and supported by the results and the published data
- The relevance of the topic of dissertation work to its actual content
This is an original study aimed at investigation of the initial steps of the generation of the spacer precursors during initiated CRISPR adaptation in E coli. The structure of experiments is very logical and all three papers published by the author are devoted to the investigation of this process, which sets this thesis apart from many others where first author paper sometimes is

not connected thematically to other publications.

- The relevance of the methods used in the dissertation

Another strong feature of this dissertation is its methodological part. The author developed an original method of primed adaptation intermediates which included sampling of short DNA fragments from E coli, cloning them into libraries with subsequent NGS sequencing. This method allowed to disclose early processes of spacer precursors generation.

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

The results were sound, extremely interesting to the CRISPR competitive community which is reflected in two publications, one in Nat Com (Detection of spacer precursors formed in vivo during primed CRISPR adaptation. Nat Commun 10, 4603) and second in Genes: Genome Maintenance Proteins Modulate Autoimmunity Mediated Primed Adaptation by the Escherichia coli Type I-E CRISPRCas System. Genes 10, 872. This paper goes further and describes Rec proteins as the major players in the process. More over, A.Shiriaeva is the first author in the invited review summarizing her research

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

This is a fundamental study of CRISPR as an immune system of bacteria. It might be applicable to the biotechnological processes where protection of the bacteria from the bacteriophage attack is important.

- The quality of publications

As discussed above, highest possible quality of publications, all on the subject of the thesis.

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

I have no major or even minor issues with the dissertation which is merely a broader narrative of two excellent experimental papers and an original review containing discussion of the own experimental data of Anna Shiriaeva

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| Provisional Recommendation |
| X <input type="checkbox"/> <i>I recommend that the candidate should defend the thesis by means of a formal thesis defense</i> |
| <input type="checkbox"/> <i>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</i> |
| <input type="checkbox"/> <i>The thesis is not acceptable and I recommend that the candidate be exempt from the formal thesis defense</i> |