

Jury Member Report – Doctor of Philosophy thesis.


Name of Candidate: Iana Fedorova

PhD Program: Life Sciences

Title of Thesis: Characterization and application of CRISPR-Cas enzymes

Supervisor: Professor Konstantin Severinov

Name of the Reviewer: Konstantin Lukyanov

I confirm the absence of any conflict of interest	Signature:  Date: 15-08-2020
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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 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

Dissertation work by Iana Fedorova is devoted to the study of the CRISPR-Cas bacterial adaptive immunity systems. A keen attention of researchers to this topic is associated not only with the fundamental interest to diverse molecular mechanisms of these systems but also with the wide practical applicability of CRISPR-Cas systems to genome editing, regulation of gene expression, labeling of genome loci, etc.

In this work, Iana performed detailed biochemical characterization of several CRISPR-Cas systems of different types from unusual bacterial sources (such as deep sea thermophilic bacteria). Another focus of research was comprehensive characterization of PAM sequences. In addition, unusual Cas12a proteins capable to process pre-crRNA without assistance of other enzymes were discovered and then used to create a multiplex gene editing system for mammalian cells. Finally, mechanism of acquisition of new spacers during adaptation was studied.

Iana used a variety of methods, from biochemical characterization of enzymes to high-throughput sequencing.

Dissertation of Iana Fedorova is published in an impressive list of top-ranked journals. Iana has two papers in Nucleic Acids Research (IF 11.5) with the first authorship. She is also the last (senior) author of the paper in RNA Biology (IF 5.4). Finally, Iana's pieces of work were included in papers published in Cell (IF 38.6), Nature Biotechnology (IF 36.6), and Nature Communications (IF 12.1).

Literature review is rather concise, well focused and nicely illustrated (12 Figures).

Results section is organized as six Chapters corresponding to the published papers. Each Chapter consists of brief scientific introduction and detailed description of the author's contribution, followed by the journal paper itself (full text plus supplementary).

To conclude, this is a top-quality work, which combines both cutting-edge fundamental science and exciting perspectives of practical biomedical applications.

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