

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Daria Artamonova

PhD Program: Life Sciences

Title of Thesis: Comparative Analysis of the Action of Eubacterial Class 1 CRISPR-Cas Systems.

Supervisor: Professor Konstantin Severinov

Chair of PhD defense Jury: Professor Yuri Kotelevtsev

Email: y.kotelevtsev@skoltech.ru

Date of Thesis Defense: October 24, 2017

Name of Reviewer: Yuri Kotelevtsev

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|---|---|
| I confirm the absence of any conflict of interest | Signature: |
| (Alternatively, Reviewer can formulate a possible conflict) |  |
| | Date: 25-09-2017 |

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 forward a completed copy of this report to the Chair of the Jury 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 of D. Artamonova (Vorontsova) is devoted to investigation of functional specificity and molecular mechanisms of adaptation in type I and type III CRISPR systems. Those two systems are more complex, include several polypeptides in final effector machinery and less studied, then type II system. The author generated a platform for investigation of the I-F CRISPR-Cas system from *P. aeruginosa* PA14 on *E. coli* strain BL21-AI background. This system was used elegantly to investigate requirements for acquirement of protospacers and of phenomenon of adaptation. In the second part study of III-A and III-B subtype CRISPR-Cas system was performed.
- *The relevancy of the topic of dissertation work to its actual content*

The topic of the dissertation is highly relevant to its content. The logic of evaluation of the results and comparison and the published data is deep and extensive.

- *The relevancy of the methods used in the dissertation*

The author used a spectrum of the methods of modern molecular microbiology, including molecular cloning of complex constructs, site directed mutagenesis and high throughput new generation sequencing.

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

All this allowed to obtain novel results and describe mechanistic features of type I and type III systems which are important to understanding of evolution and adaptation of CRISPR mechanism of bacterial defense

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

This is not obvious for me at the moment, but further investigation most likely may lead to IP applicable to CRISPR technology, which is widely used for genome editing, virus detection, directed mutagenesis in vivo

- *The quality of publications*

Both publications are of highest quality with impact factor 9+ and 10+. Daria is the first author in NAR, which is the leading specialist journal in CRISPR research

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

Minor remark is to the style of figure legends. In many cases they are lapidary which makes it somehow difficult to analyze the data without referring to the main body of the text. I would recommend to expand figure legends where necessary.

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