Skoltech
Skolkovo Institute of Science and Technology

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Aleksandra Strotskaya

PhD Program: Life Sciences

Title of Thesis: Effects of Targeting by the *Esherichia coli* I-E CRISPR-Cas System on Infection by Various Phages.

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: Petr Sergiev

I confirm the absence of any conflict of interest (Alternatively, Reviewer can formulate a possible conflict)	**Signature:**  **Date: 06-09-2017**

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 relevancy of the topic of dissertation work to its actual content
- The relevancy 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

CRISPR/Cas system is an adaptive immune system of bacteria and archaea. Molecular mechanism underlying the function of this system is of great interest to the scientific community due to the high value for the fundamental as well as applied research. The dissertation is nicely structured and clearly written. The literature review is informative and up to date. The questions addressed in the dissertation are related to the efficiency of CRISPR Cas system in the defense of bacteria against infection by a number of phages. The set of phages was selected to cover several clades with different genome organization and dynamics of DNA injection, the replication strategies and chemical structure of DNA (modified or natural).

First of all, author developed an elegant system for creation of strains carrying CRISPR spacers against selected phages. The strategy utilized a phenomenon of primed adaptation, so a plasmid with an insert of phage DNA is used to transform bacteria carrying a spacer targeting a partially complementary site in the plasmid DNA. In this way author obtained a large set of strains each of those carried a spacer against phage DNA. Each of the strains was tested for efficiency of transformation by plasmid and infection by a corresponding phage both in bulk culture and lawn. An unexpected result was that phages susceptibility to CRISPR inhibition was dramatically different as well as the recovery of escape phages. An interesting finding was also partial degradation of T7 DNA by CRISPR Cas system.

Results of the thesis were published in a number of papers in respectable scientific journals. There are no doubt in the high impact of this research on the scientific field.

Provisional Recommendation

V *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*