Skoltech
Skolkovo Institute of Science and Technology

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Julia Gordeeva

PhD Program: Life Sciences

Title of Thesis: Recognition strategies of Type I and Type V BREX systems

Supervisor: Professor Konstantin Severinov

Name of the Reviewer: Professor Yuri Kotelevtsev

I confirm the absence of any conflict of interest (Alternatively, Reviewer can formulate a possible conflict)	**Date: 12-08-2022**

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 dissertation is well written in canonical way. It contains 90 pages, 26 Figures of which 15 expanded figures present major results of the study and 6 Tables. The literature review is well written and sets the state of the art of the functional role of BREX I and BREXV systems. The review logically leads to the aims and goals of the experimental study. The Materials and Methods section is written clearly and allows thorough reproduction of the results. Results are well presented and appropriately discussed. Conclusions are supported by the results.

The relevance of the topic of dissertation work to its actual content

The content of the dissertation consists of original experiments discovering the mechanisms of BREX defense in bacterial cells, particularly the mechanisms of non self DN~ recognition strategies and also to the mechanisms of immunity to BREX defense. The content is completely relevant to the topic of the dissertation.

- The relevance of the methods used in the dissertation

  Author applied a plethora of modern methods of molecular biology including modern methods of molecular cloning and genetic engineering in procariots, kinetic analysis of growing cultures, lysogenization assay, fluorescence microscopy, Pacific Bioscience sequencing. The candidate demonstrates good understanding of all these methods, ability to present results in professional way and makes adequate conclusions.
- The scientific significance of the results obtained and their compliance with the international level and current state of the art

Several essential results were obtained in the dissertation:
BREX$_{Ec}$/BREX$_{HAR}$ gene composition in defensive and methylation complexes were identified;

brx-mediated modifications were described for the first time;
BREX$_{Ec}$ degradation activity evidence was obtained;
recognition strategies for BREX$_{Ec}$ and BREX$_{HAR}$ were proposed
toxicity of BREX$_{Ec}$ gene deletions and its effects of individual brx genes on cell growth was evaluated.

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

  This thesis is a piece of fundamental research into phage bacterial interactions. It describes a novel mechanism based on methylation of DNA. However, it is highly plausible that discovered methyltransferases will be developed into the tools for epigenetic modification of mammalian genome. This can be a novel approach for mammalian genome editing with the purpose of medical and agricultural applications.
- The quality of publications

Publications are of highest quality, with the main publication describing the results of the thesis in NAR 2019 and NAR 2020

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

I have no issues to be addressed

Provisional Recommendation

☐ **X *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*