Skoltech
Skolkovo Institute of Science and Technology

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Sergey Shmakov

PhD Program: Life Sciences

Title of Thesis: Computational approaches for discovery of novel CRISPR-Cas systems

Supervisor: Professor Konstantin Severinov

Chair of PhD defence Jury: Professor Mikhail Gelfand ***Email:*** *M.Gelfand@skoltech.ru*

Date of Thesis defence: October 16, 2017

Name of Reviewer: Mikhail Gelfand

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

The purpose of this report is to obtain an independent review from the members of PhD defence Jury before the thesis defence. The members of the PhD defence Jury are asked to forward a completed copy of this report to the Chair of the Jury at least 30 days prior the thesis defence. The Reviewers are asked to bring a copy of the completed report to the thesis defence and to discuss the contents of each report with each other before the thesis defence.

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 title 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

The problem addressed in the dissertation is one of the hot topics in modern molecular biology and bioinformatics due to its evolutionary significance — some, including the supervisors of this project, claim that CRISPR-Cas systems are the first real example of Lamarckian evolution; I would not go that far, but they are clearly the first example of adaptive immunity in prokaryotes — and its practical applications in genome editing. Hence, the search for new types of CRISPR-Cas systems is important both for theoretical and practical reasons, as they would inevitably yield better understanding of the evolution of adaptive immunity and may provide better, or at least, additional tools for gene engineering.

The project was well designed and implemented at a high professional level, and it produced important, valuable, and reliable results, as follows from independent downstream validation in experiment. Importantly, not only new types of CRISPR-Cas systems were identified, but new functions and mechanisms of action of these systems were predicted, mainly based on protein sequence and structure analysis and comparative genomics. The new findings were so huge that required revision of the CRISPR-Cas nomenclature and, on the other hand, allowed the author to suggest an evolutionary scenario for Class 2 systems.

The thesis is generally clear and well written, although not free from misprints and some language errors. In particular, Latin species names are not italicised.

The review section, while rather short, is sufficiently detailed and follows a clear logic. It gives a good picture of the field and covers most of the relevant sources.

The methods are adequate, and a computational pipeline has been implemented using both standard and ad hoc programs. Nothing is said about its availability, though.

The level of publications is exceptionally high, including first author publications in top journals. The results have been reported at major international conferences.

Provisional Recommendation

☒ *I recommend that the candidate should defend the thesis by means of a formal thesis defence*

☐ *I recommend that the candidate should defend the thesis by means of a formal thesis defence 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 defence*