

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 defense Jury: Professor Mikhail Gelfand

Email: mikhail.gelfand@gmail.com

Date of Thesis Defense: October 16, 2017

Name of Reviewer: Blake Wiedenheft

| | |
|---|---|
| <p>I confirm the absence of any conflict of interest</p> <p>(Alternatively, Reviewer can formulate a possible conflict)</p> | <p>Signature:</p>  <p>Date: 23-09-2017</p> |
|---|---|

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

The work described in this thesis aims to expand the phylogenetic and functional diversity of Class 2 CRISPR-Cas systems. In nature, these systems are part of an RNA-guided adaptive immune system, but mechanistic insights determined using a combination of biochemical, genetic, and structural techniques has led to the creative repurposing of these enzymes for applications that nature never intended. Class 2 CRISPR systems are now routinely used for programmable genome engineering in a wide range of organisms; including humans, where they have recently been used in clinical application to treat genetic diseases.

In this thesis, the author opens with a concise summary of the previous work performed on CRISPR-Cas systems, and then identifies existing gaps in our knowledge and limitations of previously performed phylogenetic studies. The author then explains how he developed a computational pipeline designed to identify new CRISPR-Cas systems in expanded databases and how this pipeline was implemented to identify six new CRISPR-Cas subtypes. This project was well-conceived, the experiments have been professionally executed, the results are clearly articulated, and conclusion are well-supported. This assessment is supported by an extensive and impressive list of peer review publications.

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