

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:

<p>I confirm the absence of any conflict of interest</p> <p>(Alternatively, Reviewer can formulate a possible conflict)</p>	<p>Signature: Georgii A. Bazykin</p>  <p>Date: 16-10-2017</p>
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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 thesis represents a breakthrough of substantial magnitude in the hot field of CRISPR research. Using a range of computational approaches, Mr. Shmakov has significantly expanded the diversity of known CRISPR-Cas systems, describing 11 new major types of class 2 systems, in addition to the four systems known previously. The computational methods used appear appropriate, and some of the predictions have already been validated experimentally. In particular, he described a tentative set of systems lacking the adaptation module (cas1 or cas2), which was only possible using the novel CRISPR array search-based computational approach. In addition to this major result, the thesis also advances understanding of the evolutionary origin of several CRISPR-Cas classes as well as of selection affecting these systems.

The results of the thesis are published in four papers in top of the line journals, including *Science* and *Mol Cell*. The text is concise and clear, and contains few typos. As described in detail in the thesis, the results, especially the characterization of the RNA-targeting C2c2 effector, may be of substantial applied value.

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