

## Jury Member Report – Doctor of Philosophy thesis.

**Name of Candidate:** Sofia Medvedeva

**PhD Program:** Life Sciences

**Title of Thesis:** Natural diversity of CRISPR spacers

**Supervisor:** Prof. Konstantin Severinov

**Co-Supervisor:** Dr. Mart Krupovic

**Chair of PhD defense Jury:** Prof. Mikhail Gelfand


**Email:** [m.gelfand@skoltech.ru](mailto:m.gelfand@skoltech.ru)

**Co-Chair of PhD defense Jury:** Prof. Guennadi Sezonov

**Email:** [guennadi.sezonov@sorbonne-universite.fr](mailto:guennadi.sezonov@sorbonne-universite.fr)

**Date of Thesis Defense:** 3 June 2019

**Name of the Reviewer:**

<p>I confirm the absence of any conflict of interest</p> <p>(Alternatively, Reviewer can formulate a possible conflict)</p>	<p><b>Signature:</b></p>  <p><b>Date: 03-05-2019</b></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 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 relevance of the topic 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 thesis manuscript presented by Sofia Medvedeva gathers works on CRISPR-Cas systems, with a particular focus on the diversity of spacer content. CRISPR-Cas systems are the adaptive immune system of bacteria and archaea. They are able to build a memory of past encounters with foreign genetic elements through the capture of small DNA fragments as spacers between repeats. The study of these spacers can thus offer insights into gene transfer occurring in microbial populations and in particular the dynamics of viral infections.

Sofia Medvedeva first offers a brief introduction to CRISPR-Cas systems. The results section consists in 5 published papers to which she contributed, including one as a co-first author, as well as an unpublished manuscript as a first author. Finally Sofia briefly summarises and discusses her results to conclude her manuscript.

While some studies of CRISPR spacer diversity have already been conducted, Sofia Medvedeva nicely shows how their systematic study in microbial populations can yield new insights. In particular, the presence of varying or shared spacers between geographically distant populations and through time can hint at difference in CRISPR dynamics between species and niches as well as global transfer of microbes. An interesting finding of this PhD thesis is the description of Sulfolobus viruses carrying short CRISPR arrays that target other viruses, and how these CRISPR arrays seem to impact the coevolution of Sulfolobus and their viruses. Similarly, mobile genetic elements of thaumarchaea were observed to carry CRISPR arrays targeting other mobile elements, highlighting the role that CRISPR-Cas systems can have in controlling horizontal gene transfer.

Altogether the research methodology is appropriate. The interesting results gathered by Sofia Medvedeva contribute to further our understanding of CRISPR spacer diversity and what can be learned from its study, they also open new research directions. With this work, Sofia Medvedeva demonstrates a strong bioinformatics expertise, an in depth understanding of CRISPR-Cas systems, and her ability to conduct rigorous research. I therefore believe that she deserves the grade of PhD and should defend her thesis.

#### **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*