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Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: MEDVEDEVA Sofia

PhD Program: Life Sciences

Title of Thesis: Natural diversity of CRISPR spacers

Supervisor: K Severinov, M. Krupovic

Chair of PhD defense Jury: G Sezonov ***Email:*** *guennadi.sezonov@sorbonne-universite.fr*

Date of Thesis Defense: 03/06/2019

Name of the Reviewer: Guenandi Sezonov

I confirm the absence of any conflict of interest	**Signature:**  **Date: 19-04-2019**

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

The Thesis submitted by Sofia Medvedeva explores the diversity of CRISPR spacers (CRISPRome) in different natural prokaryotic communities from the microbiome of a mammoth intestine to *Thermus* and Sulfolobales communities from distant hot springs in Italy, Chile and Japan.

The thesis quality is excellent and the obtained results are significant and very original. The work presented by S. Medvedeva makes a significant contribution to our knowledge of a diversity of information carried by CRISPR networks and allows to gain important insights in virus-host interactions in different microbial communities.

The structure of the manuscript is logical and well adapted to the presented results. The brief introduction summarizes well the essential points concerning structural organization of CRISPR-Cas systems and their functioning. All essential publications from the CRISPR domain are well cited and the list of the references includes recent publications. The six Chapters include all papers published or submitted. The manuscript is finished by a Conclusions/Perspectives section that includes a short discussion of the obtained results and summarizes the importance of the obtained data and indicates future directions of this research.

Generally speaking, the thesis's content is perfectly relevant to the thesis topic.
The methods used in the dissertation are fully relevant, modern, original and well appropriated for the aims of the study. The obtained results were analyzed correctly and all conclusions made are well supported by the data.
The results obtained during the PhD training of Sofia Medvedeva make an essential contribution to our knowledge of the virosphere in general. The analysis of CRISPR spacers is a valuable source of information on virus-host interactions, since they correspond to short fragments of virus DNA previously encountered and "registered" in CRISPR loci. Such an analysis can be particularly valuable when applied to metagenomic data where the CRISPR spacers can be used to identify the viral sequences and to detect the species drift in viral populations. This diversity of the CRISPR spacers in different natural prokaryotic populations was analyzed in this thesis using the modern PCR/NGS technology on contemporary or extinct prokaryotic populations.
The results of the different CRISPRomes analyses allowed to answer several important biological questions concerning (1) the extent of diversity of CRISPR spacers; (2) the short- and long-term dynamics of spacer sequence diversity; (3) influence of geographical isolation on the diversity of spacers; (4) role of CRISPR in the immunity of natural prokaryotic population against local viruses.
The results are published in 5 high impact international scientific journals with an additional manuscript submitted. The quality of these publications is very high.
To conclude, the quality and scientific impact of S. Medcedeva's thesis, made in two different teams in Russia and in France, could be considered as outstanding and I can rate it in the 10% of the best thesis I reviewed during my scientific career.

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 the 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.*