To the Chairman of Scientific jury appointed by Order No. 583/01.12.2023 of the Director of the NCZPB

 НАЦИОНАЛЯВ ЦЕЕТЪР ПО ЗАРАЈНИ И НАРАЗИТНИ БОЛЕСТИ
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## REVIEW

by AssocProf. Dimitar Ivanov Vasilev,PhD., FMI, SU St. Kliment Ohridski of a dissertation, on the topic:

Microbiome and bioinformatics analysis to study the pathogenesis of sarcoidosis

with author Yordan Krasimirov Hodzhev, full-time doctoral student at

## NATIONAL CENTER FOR INFECTIOUS AND PARASITIC DISEASES

Department of "Microbiology", laboratory "Especially dangerous bacterial infections" (OBI) Sector "Microbiome"

supervisor:

Prof. Dr. Stefan Panayotov,

for the defense of a dissertation for awarding the educational and scientific degree 'doctor' in the field of higher education - 4. Natural sciences, mathematics and informatics, professional direction - 4.3. Biological sciences, PhD program Microbiology....... scientific specialty 01.06.12 Microbiology

The work presented by Yordan Hodjev was written in accordance with Art. 36 (1) of the Regulations for the Development of the Academic Staff of the NCZPB. It includes the necessary documents complying with the regulations for the procedure for the defense of a dissertation, such as:

- curriculum vitae in European format;
- minutes from the NUS of the NCZPB and at the first meeting of the scientific jury, related to reporting the process and the readiness to defend the dissertation work;
- dissertation work;
- project for an abstract;
- a list and copies of scientific publications on the subject of the dissertation,
- participation and work in projects,
- declaration of originality, and
- a reference to the specific requirements of the NACID.

The PhD student has submitted 6 publications, one of which was published in co-authorship in the refereed prestigious scientific journal Frontiers in Microbiology, as well as in MDPI

Microorganisms with a total Impact Factor of 17.59, as well as 22 presentations of reports, posters at national and international conferences.

Yordan Hodjev has a master's degree in "molecular biology" from the Faculty of Biology of Sofia University "St. Kliment Ohridski". He began to deal with bioinformatics during his studies and work as a full-time doctoral student at the Department of Microbiology, NCSPB. The work presented by Yordan Hodjev is written on 128 pages, standard structured (A4 format) and includes; Literature review; Goals and tasks; Materials and methods; Results, Discussion of the results, Conclusions, Contributions as well as Conclusion. The results are presented in the form of tables and figures. Thus, the presented text of the dissertation includes 24 figures and 10 tables. The list of cited literature includes 121 articles, and a significant part of them are after 2010.

The aim of the study is to apply bioinformatics approaches to clarify the pathogenesis of the disease sarcoidosis. Microbiome in patients with pulmonary sarcoidosis is the object of research. Sequencing data from clinical materials from blood, BAL and biopsy material were analyzed. Modern approaches and methodology for bioinformatic and biostatistical analysis of sequencing data are applied.

Data from metagenomic and target sequenced samples were analyzed. The quality of sequencing, assembly and annotation was assessed. One of the greatest merits of the presented dissertation is the use of different software programs and platforms, as well as their comparison. The implementation of all these analysis procedures have a large applied aspect and have contributed to the achievement of a high quality of skills and knowledge by the PhD student. This will undoubtedly have a positive impact on the development of the NCSPB and the Department of Microbiology in the field of bioinformatic analysis of sequencing data. Particularly original (even this can be defined as a significant contribution of the work, a machine learning method based on a classification tree of decisions was used to successfully distinguish sarcoid patients from a control group of healthy individuals, using data from previous experiments with the aim to supplement and extend information on the potential contribution of the described microbial types and genera to the pathogenesis of sarcoidosis. Decision tree visualization provides insight into the decision-making process. In the introduction, which occupies one page, an annotation of the work itself is made, and the results of the work are presented succinctly. I believe that it would be better in such an introductory part of a dissertation work to briefly present the setting of the work and the expected results.

The "Literature review" section occupies 20 pages and includes an overview of the literary sources used by the dissertation student. A comparative review of the methods for researching the etiology, diagnosis, epidemiology and infectious hypothesis for the occurrence of sarcoidosis was made.

The section "Goals and tasks" is described briefly and without additional explanations, but it is in harmony with the idea and statement of work. The goals and objectives themselves are presented well without any discrepancy with what is presented as the content of the results and the framing of the conclusions. I believe that the doctoral student Yordan Hodzhev has fulfilled the set goals and tasks

The chapter "Materials and methods" gives the best information about the possibilities and knowledge of the doctoral student. Despite the interesting presentation of methods and software tools for analysis, which appears at first glance to be documentation for the use of

## CONCLUSION

The presented dissertation work has a certain contribution character: an interesting object of research, new methods of analysis, many new and interesting results, the main part of the work has been published in many good journals. All this, as well as what I wrote above in the review of the work, gives me reason to support with fullconfidence the awarding of the educational and scientific degree "Doctor" to Yordan Krasimirov Hodjev based on the dissertation work presented by him.

Sofia, 09.01.2024 Prepared the review: Assoc. Dr. Dimitar Iv. Vassilev