



STATEMENT

On the Dissertation of **Yordan Krasimirov Hodzhev**
for the awarding of the educational and scientific degree "Doctor
of Philosophy" in professional direction 4.3. Biological
Sciences, PhD Program "Microbiology"
entitled: "**Microbiome and bioinformatics analysis to study the pathogenesis of sarcoidosis**"

By Assoc. Prof. Georgi Yordanov, DSc, from the Faculty of Chemistry and Pharmacy – SU,
appointed for a **member of the scientific committee** according to Order of the Director of
NCIPD # 583/01.12.2023.

The presented dissertation of Yordan Krasimirov Hodzhev is entitled "Microbiome and bioinformatics analysis for the study of the pathogenesis of sarcoidosis", is written on 138 pages, contains 24 figures and 10 tables, and 121 literature sources are cited. In terms of volume, structure and design, the dissertation fully meets the requirements for obtaining the educational and scientific degree "Doctor of Philosophy".

The aim of the dissertation is to conduct a microbiome and bioinformatics analysis to establish a relationship between the blood microbiome and the pathogenesis of pulmonary sarcoidosis. The topic of the dissertation falls into the field of research and analysis of the microbiome in normal and pathological conditions, which is an extremely fast-developing, up-to-date and markedly interdisciplinary scientific field, uniting different parts of microbiology, informatics and medicine and revealing numerous possibilities for applications. It is noteworthy that the doctoral student successfully demonstrated the mastery of knowledge and skills from various sciences with a view to achieving the goal set in the dissertation.

The literature review and the presented results in the dissertation work are in full accordance with the clearly set goal and the correctly defined tasks for implementation. An overview of granulomatous lung diseases, the lung microbiome in normal and pathological conditions, and its suspected role in the pathogenesis of sarcoidosis is provided. The idea of a normal blood microbiome, its dynamics and approaches to analysis are presented, and the main hypothesis of the study about a possible link between the dysbiosis of the blood microbiome and the pathogenesis of sarcoidosis is presented. The different concepts regarding the origin of microbial DNA in the blood of clinically healthy individuals are described. The general impression is that the doctoral student has a good literary awareness of the subject. The experimental part gives a detailed and correct description of the experimental procedures used and the data processing carried out. In the course of the work on the dissertation, the doctoral student became familiar with microbiological and bioinformatics experimental methods, which were well combined in the conducted research and gave the opportunity to obtain interesting results about the blood microbiome in healthy individuals and in patients with sarcoidosis.

The more significant scientific results and contributions of the dissertation research could be summarized as follows:

- The taxonomic composition of the blood microbiome in clinically healthy individuals was established. The presence of a fungal microbiome in the blood has been demonstrated.

- A relationship has been established between the taxonomic composition of the blood microbiome and the development of pulmonary sarcoidosis. Statistically significant increases in certain microbial taxa have been demonstrated in the blood of sarcoid patients compared to healthy individuals. Other microbial taxa are significantly reduced and some are completely absent in patients with sarcoidosis.

- Methods for visualization and assessment of the quantitative and qualitative composition of the blood microbiome are proposed. A good visual description of taxonomic content and biodiversity was achieved using Sankey and Krona diagrams.

- A machine learning classification model is proposed to identify the taxa most likely to contribute to the pathogenesis of sarcoidosis.

The overall impression of the dissertation is that a systematic and precise research work has been carried out, and the aims and objectives of the dissertation work have been achieved. The thesis is well laid out and clearly written. The results obtained for the blood microbiome in normal and pathological conditions are interesting and encouraging, and a similar type of research can certainly be continued in the future and expanded in relation to other systemic chronic diseases, as well as the effect of applied pharmacotherapies on the taxonomic composition. The methodology could be refined and improved by fractionating the blood cells and establishing the distribution of microorganisms from the different taxonomic units in the different types of blood cells, which would shed further light not only on the biodiversity, but also on the distribution of the microbiota in the different blood cells. I believe that this dissertation is of interest both to narrow specialists in microbiome and bioinformatics and to specialists in various other fields related to biomedicine.

The autoreferat complies with the requirements and correctly reflects the content of the dissertation and the contributions of the research included in it.

The results of the dissertation work are contained in 7 scientific publications, of which three in Q1 journals, one article in Q2, one in Q3 journal, and two articles in Q4 journals, which is a confirmation of the high level of research. In one of the publications, the PhD student is the sole author, and in three other publications he is the first author, which is a testimony to his leading participation and contribution. The results of the doctoral student's research have been presented in an impressively large number of reports at international and national scientific forums - 22.

Conclusion: Yordan Hodzhev's dissertation fulfills the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria and the Regulations for the Implementation of that law. He has acquired the necessary level of scientific competence in the field of microbiology and data processing, in which he has obtained interesting and valuable scientific results. Based on this, I give a positive assessment and strongly recommend to the Honorable Scientific Jury to vote for awarding the educational and scientific degree "Doctor of

Philosophy" in professional field 4.3 "Biological Sciences" (Microbiology) to Yordan Krasimirov Hodzhev.

Signature:

(Assoc. Prof. Georgi Yordanov, DSc)

08.01.2024