



STATEMENT

by Assoc. Prof. Nikolay Yanev, MD, PhD, Medical University - Sofia, on a dissertation work for the acquisition of the educational and scientific degree "Doctor" in the specialty "Microbiology" (code 01.06.12) from professional direction 4.3 "Biological Sciences" on the topic

"Microbiome and bioinformatics analysis to study the pathogenesis of sarcoidosis with author Yordan Hodjev.

I declare that I have no conflict of interest within the meaning of art. 4, para. 5 of Law on the Development of the Academic Staff in the Republic of Bulgaria. I have joint publications with Yordan Hodjev, having been involved in providing clinical materials, but had no involvement in the development and results of the dissertation work.

The review was prepared in accordance with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria and the Regulations on the Terms and Conditions for Acquiring Scientific Degrees at the National Center of Infectious and Parasitic Diseases

The submitted documents are in accordance with the instructions published in the Regulations for the Implementation of the Law on the Development of the Academic Staff in the Republic of Bulgaria and the internal Regulations for the conditions and procedures for acquiring scientific degrees at the National Center of Infectious and Parasitic Diseases

Relevance of the topic

The study aimed to determine the potential causal relationships between blood microbiome dysbiosis in pulmonary sarcoidosis. Such research is current and innovative. The dissertation aims to develop and apply (1) modern bioinformatics tools for sequencing data processing; (2) to apply more efficient methods to visualize data from single patients, and (3) to apply machine learning algorithms to identify key microbial taxa with potential contributions to the pathology of pulmonary sarcoidosis.

The literature review shows a good awareness of the problem. Current methodical approaches for the study of sarcoidosis and other granulomatous diseases with bioinformatic and biostatistical methods are described. The review includes an up-to-date literature reference.

The aim of the dissertation work is clearly formulated and includes tasks that are scientifically based, feasible and correspond to the goal set to be achieved.

Research methods include bioinformatic and biostatistical analyzes and have a key role in investigating changes in microbiome composition. The proposed methods of data visualization are suitable for the purposes of the study. The proposed method for the classification of microorganisms relevant to the pathogenesis of sarcoidosis is innovative. The proposed approaches enable the analysis and interpretation of large arrays of sequencing data, aiming to identify nuances of dysbiosis in the blood microbiome of patients with sarcoidosis.

The results include entirely self-conducted studies. The obtained results are significant and have a contribution to the study and confirmation of the microbial hypothesis for the etiology of sarcoidosis.

The discussion of the obtained results is on a professional basis and with a critical evaluation of the research. The obtained results are compared with published results of the leading researchers in the field.

The conclusions and contributions are in accordance with the obtained results and the set aims and objectives.

The scientific achievements could be summarized as follows:

1. Quantitative assessment of the dysbiosis of the blood microbiome is an indicator of the development of pathological processes.

2. A bioinformatic approach was developed for microbiome analysis of total microbial DNA from bronchoalveolar lavage, blood and tissue samples. Microbial communities specific to pulmonary sarcoidosis have been identified.

3. Methods for visualization and evaluation of the quantitative and qualitative composition of the blood microbiome of individual patients are proposed.

4. The applied machine learning classification model enables identification of key microbial taxa most likely to contribute to the pathogenesis of sarcoidosis

On the topic of the dissertation, the doctoral student Yordan Hodjev applies six articles in journals with impact factor and impact rank. Attached is a cited poster in a journal with an impact factor, which, according to Appendix 1 of the Regulations of the National Center for the Implementation of the Law on the Development of Academic Staff, is equated to publications with an impact factor. The total impact factor is 22.559. The number of citations is 14. The number of credit points is 1239 and many times exceeds the requirements of National Centre For Information And Documentation for the educational and scientific degree "doctor".

I have no critical remarks about the planning, objectives, results and conclusions of the dissertation work.

In conclusion, the dissertation meets the mandatory and specific conditions and scientometric criteria of the Law on the Development of the Academic Staff in the Republic of Bulgaria and the Regulations to it.

I confidently give my **positive assessment** and recommend to the Scientific Jury to award the acquisition of the educational and scientific degree "Doctor" to Yordan Hodjev in the specialty "Microbiology" (code 01.06.12) from Professional Direction 4.3 "Biological Sciences".

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