

To Scientific jury,
defined by Order P-109-41/ 21.01.2022
of the Rector of the Medical University
"Prof. P. Stoyanov" – Varna
Prof. Valentin Ignatov, MD, PhD

On your protocol №1/27.01.2022

I present attached:

OPINION

on dissertation for the award of educational and scientific degree "Doctor"

by Assoc. Prof. Deyan Lyudmilov Dzhankov, MD, PhD, Associate Professor at the Department of General and Clinical Pathology, Forensic Medicine and Deontology at MU "Prof. Dr. Paraskev Stoyanov" – Varna
Appointed a member of the Scientific Jury / order № P-109-41/ 21.01.2022 of the Rector of MU "Prof. P. Stoyanov" – Prof. Dr. Valentin Ignatov, MD

Field of higher education 7. Health and sports. Professional direction 7.1 Medicine. Scientific specialty 03.01.03 "Pathoanatomy and cytopathology".

Topic: " IMMUNOHISTOCHEMICAL EXPRESSION OF THE MARKER FOR RIPK3 NECROPTOSIS IN BREAST CANCER "

Author: Martina Georgieva Stoeva

Form of doctoral studies: full-time form

Department: General and Clinical Pathology, Forensic Medicine and Deontology

Scientific adviser: Prof. Maria Tsaneva, MD, PhD

I. **Brief biographical data on the candidate's career development**

Dr. Martina Georgieva Stoeva graduated from Mathematical High School "Dr. Peter Beron" in Varna in 2006 and graduated with a master's degree in medicine at the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna in 2012. In 2013 she began his professional career as a specialist at the Clinic of General and Clinical Pathology, Sveta Marina Hospital, Varna. Since 2015 is a part-time assistant, and in 2017. was appointed after a competition and as an assistant in the Department of General and Clinical Pathology, Forensic Medicine and Deontology at MU "Prof. Dr. Paraskev Stoyanov" – Varna. From the beginning of 2018 he acquired a specialty in "General and Clinical Pathology".

As an assistant Dr. Stoeva participates in the educational work of the Department, conducts practical classes in General and Clinical Pathology of physicians and dentists in Bulgarian and English, pharmacists and laboratory technicians in Bulgarian.

Dr. Stoeva was enrolled with order № P-109-39 / 01.02.2019 for full-time doctoral studies on "Expression of immunohistochemical markers for necroptosis in breast cancer" with subsequent correction of the topic with order № P-109-439 / 07.10.2021, adding a specific marker associated with necroptosis-RIPK3. In connection with his dissertation he has two full-text publications in a Bulgarian journal and participation with a report in a scientific conference in Bulgaria.

Dr. Stoeva is a member of the Bulgarian Society of Pathology and a member of the Faculty Council at the Dean of Medicine at the Medical University of Varna.

II. General performance of the candidate

The presented materials on electronic and paper media meet the requirements of the Regulations for the development of the academic staff at MU Varna from 2018 under the Procedure for acquiring ONS "Doctor" at MU Varna. The doctoral student passed the exam for doctoral minimum in the specialty "General and Clinical Pathology" on 28.09.2020 with a very good grade. The required scientometric indicators are covered. The doctoral student was dismissed with the right to defense by Order № P-109-41 of 21.01.2022.

III. Dissertation evaluation

The dissertation on "Immunohistochemical expression of the marker for necroptosis RIPK3 in breast cancer" is well structured with different basic elements: literature review, purpose and objectives, research materials and methods, results, discussion, conclusions, contributions and bibliography. It is written on 133 standard pages and is illustrated with 50 tables and 42 figures, and the literature sources include 205 titles, of which 4 in Cyrillic and 201 in Latin.

The topic of the dissertation is related with the most common malignant tumor in female - breast cancer, looking for a biomarker for necroptosis in tumor tissue in order to predict biological behavior of the tumor and the possibility of therapeutic response. The literature review is comprehensive, up-to-date, the epidemiology has been presented in details, risk factors, morphological characteristics with prognostic and predictive parameters, as well as methods of treatment of mammary carcinoma are also well studied.

There is significant progress in medical science in the treatment of mammary carcinomas, which is associated with the disclosure of their molecular profile by establishing hormonal receptor status, proliferative index and overexpression of growth factor. Despite the implementation of these characteristics in the diagnosis associated with the treatment of mammary neoplasms, some of the tumors represent a significant therapeutic problem in terms of recurrence and metastasis.

A good possibility for the prognosis of these tumors is the study of molecular biomarkers with prognostic and predictive potential, as may be the necroptotic factor-RIPK3 used in the present study for mammary carcinoma.

In search of such an approach, the phd student has set the ambitious task to study the immunohistochemical expression of the biomarker in tumor cells and the possible correlation of the results with the aggressiveness of the tumor, respectively the likelihood of metastasis. The difference in expression in non-tumor and in neoplastic cells is also presented, as well as the relationship of the latter with the clinical and morphological parameters of tumors.

The set goal is clearly and specifically defined. The formulated tasks are logical and feasible. The used methods are modern, consistent with the purpose and the objectives.

The results are systematically described, logically arranged in the order of their receipt. The results obtained are original. In the discussion a thorough comparison of the obtained results with the data published in the literature was made. The conclusions are clearly formulated, and some of the contributions of the dissertation have a practical-applied nature.

Personally, I am curious to see if there is a correlation in the biological behavior of mammary carcinomas dependent on the expression of the biomarker RIPK3 in the nuclei and / or cytoplasm of tumor cells versus morphological parameters such as tumor necrosis that has an identical morphology as necroptosis and stromal lymphocyte infiltration in tumor tissue due to the presumed increased immunogenicity of malignant neoplasms with higher RIPK3 expression.

IV. Evaluation of publications and personal contribution of the PhD student

Dr. Stoeva is the author of 2 full-text publications in Bulgarian journals, being the only author in one of them and the first author in the second publication, he also participated as the first author in a scientific conference.

V. Abstract

The abstract of the dissertation is prepared in accordance with the requirements of the Regulations of the Academic Staff of MU-Varna, reflecting adequately and sufficiently the state of the studied problem, the set aim and experimental tasks, the methods used for their practical implementation, the results obtained, their analytical description and interpretation of own data, as well as the author's conclusions and contributions.

VI. General assessment of compliance with the mandatory conditions, quantitative criteria and scientific-metric indicators, according to the Law on the Development of Academic Staff in the Republic of Bulgaria and the Regulations for its application.

The quantitative scientometric criteria for the PhD degree have been met, in accordance with the LADRB, the Regulations for its application and the Regulations of MU-Varna - a total of 30 points is required: indicator D (publications and reports) - $30+10 = 40$ points.

Conclusion

As a member of the scientific jury, I give a positive evaluation for the acquisition of the scientific degree "PhD" by Dr. Martina Georgieva Stoeva. The submitted dissertation, abstract and published scientific works meet the requirements of the Law on the Development of Academic Staff of the Republic of Bulgaria (LADRB) and the Regulations of MU-Varna. The dissertation addresses a scientifically and clinically relevant problem, and the conclusions drawn have potential for future research in the field.

21.02.2022



Assoc. Prof. Deyan Dzhenkov, MD, PhD