

REVIEW

Subject: Competition for the academic position of "Associate Professor" in the specialty "General and Clinical Pathology", professional field 7.1. Medicine, field of higher education 7. Health and Sports - two positions of 0.5 full-time position for the Department of "General and Clinical Pathology, Forensic Medicine and Deontology", Faculty of Medicine and one full-time position for the Clinic of "General and Clinical Pathology" at the University Hospital "St. Marina" EAD, announced in the State Gazette, issue 85/08.10.2024. **with candidate:** Dr. Martina Georgieva Stoeva

Reviewer: Professor Dr. Petar Ivanov Genev, MD, Department of General and Clinical Pathology, Forensic Medicine and Deontology, Medical University - Varna

1. General and biographical data

Dr. Martina Stoeva was born on 22.02.1988 in Blagoevgrad. She graduated Medicine from the Medical University of Varna and obtained a diploma with registration number 001897/15.11.2012. After graduation, she began specialization at the Clinic of General and Clinical Pathology, University Hospital "St. Marina" EAD - Varna. In 2015, she was elected as a part-time assistant at the Department of General and Clinical Pathology at the Medical University - Varna, and in 2017, as a full-time assistant. As an assistant, Dr. Stoeva participates in the teaching work at the Department - conducts practical classes in all taught disciplines with medical and dental students, including in the English-language training program. Dr. Stoeva also fully participates in the diagnostic process, gradually mastering the basic methods of biopsy practice. She obtained a specialty in "Pathoanatomy and Cytopathology" (diploma with reg. No. 021479/20.02.2018). Since 2022, she has been a chief assistant at the Department of Pathology at the Medical University - Varna.

Over the years, Dr. Stoeva has shown diverse scientific interests, primarily in the field of tumor pathology - breast and prostate carcinoma, adipose tissue pathology, molecular mechanisms of cell death, experimental morphology, casuistics. Accordingly, a large part of her publications are in this field and naturally, this is also the topic of the dissertation: Immunohistochemical expression of the necroptosis marker RIPK3 in breast carcinoma successfully defended in 2018. Dr. Stoeva makes efforts to maintain her qualifications by participating in diagnostic seminars, including the European School of Pathology organized by the European Society of Pathology, as well as for mastering methodologies and diagnostic algorithms. The management of the University Hospital "St. Marina - Varna" has issued Dr. Stoeva a Certificate for more than 7 years of work experience in the specialty.

1. General description of the submitted materials

For this competition, the candidate has submitted for review a total of 24 publications in scientific journals, distributed as follows:

- abstract of a dissertation for the award of the educational and scientific degree "doctor": Immunohistochemical expression of the necroptosis marker RIPK3 in breast carcinoma (Group of indicators A 1)
- habilitation work - monograph: Pathomorphology of prostate carcinoma Publishing House of MU - Varna, ISBN: 978-619-221-469-2 (Group of indicators B 3)
- 10 articles published in scientific journals, referenced and indexed in world-renowned databases with scientific information (Group of indicators G7)
- 6 publications in peer-reviewed journals and indexed in world-renowned databases of scientific information (Group of indicators D8)
- Reference for citations (Group of indicators D10)

2. General characteristics of the candidate's research and applied scientific activity

The dissertation studies the alternative form of cell death (necroptosis) in breast carcinoma and in particular - the expression of the necroptotic marker RIPK3 compared to the expression of the proliferative marker Ki67, the receptor status, in relation to clinical indicators, such as age, stage and progression-free survival of patients. The mechanisms of occurrence and the role of in breast carcinoma are examined. The immunohistochemical expression of appropriately selected markers for both processes are compared with clinico-morphological parameters using several assessment scales. The importance of autophagy and necroptosis for the overall survival of patients, their potential prognostic value and a profile of patients with an increased risk of death from breast cancer are discussed. It is established that low expression of RIPK3 is associated with aggressive biological behavior, while high expression of RIPK3 is associated with better survival, with the necroptosis marker being an independent prognostic factor. The dissertation is assessed at 50 points, which meets the requirements of Indicator A1.

The monograph presented as a habilitation thesis is also in the field of oncopathology. It represents an in-depth review of the normal anatomy and histology of the prostate gland and the tumor processes that arise in it. The emphasis falls on prostate cancer - etiology, modern classification, staging, determination of Gleason score and ISUP Grade groups, benign lesions, imaging diagnostics, including magnetic resonance imaging. The monograph is evaluated at 100 points, which meets the requirements of Indicator B 3.

To cover Group D indicators, Dr. Stoeva has provided for review 10 articles published in scientific journals, referenced and indexed in world-renowned databases of scientific information, another six articles in non-refereed journals and one article beyond the minimum requirements for "Associate Professor".

The first group includes:

- two articles on experimental models of the role of vitamin K in metabolic syndrome and its influence on calcium metabolism in conditions of deficiency. Both publications are joint with pharmacologist colleagues
- three large demographic studies on head and neck tumors, glial and intracranial tumors
- four case reports
- one study on the diagnostic significance of cytokeratin as an epithelial marker in the differential diagnosis of glioblastomas

The articles from the second group thematically present separate elements of the monograph, pathology of adipose tissue, salivary gland tumors and one literature review on the topic of Tetraspanin 151 and carcinogenesis.

Part of the works are in collaboration with various clinicians - they include description and morphological assessment of biopsy and experimental materials. The total score of this scientific production is 224.31 with a required minimum of 200 points. Thus, the minimum requirements of Group of indicators G are met.

The Library of the Medical University of Varna has issued an Academic Report on the publications and citations of Dr. Stoeva, which certifies that four citations have been found, corresponding to 60 points. This meets the requirements of Group of indicators D and testifies for the reflection of the candidate's scientific activity in the periodical literature.

Dr. Stoeva's publication activity thematically covers almost all areas of pathology, including molecular and experimental pathology. A large part of the scientific works are the work of authors from different medical specialties, which be considered as a proof for her ability to work in a team.

3. Assessment of the candidate's pedagogical training and activity

Medical University of Varna issues a Certificate of the academic workload of Dr. Stoeva for the last five years (Issue No. 112-476/24.10.2024), which shows that she has about 7 years of teaching

experience and has conducted an average of 250-300 hours of classes per year, including English-language teaching, with an annual standard of 220 teaching hours.

4. Main scientific and applied scientific contributions

The doctoral thesis, habilitation work, as well as thematically related full-text publications clarify various aspects at the molecular level of common oncological diseases, in particular - breast and prostate carcinoma.

The study of alternative molecular mechanisms of cell death and survival in the doctoral thesis contributes to the understanding of the role of necroptosis in the biological behavior of breast carcinoma. Enriching science with such new facts is important for clarifying carcinogenesis in other locations as well.

The habilitation work contributes to clarifying the mechanisms for the occurrence of tumors in the prostate gland.

Studies on the role of vitamin K in experimental conditions have an original contribution regarding histological changes, both for metabolic syndrome and arterial calcinosis.

An original contribution to the elucidation of the clinical symptoms of ARVD is the immunohistochemical study of neurotrophins in ectopic adipose tissue and their role in the occurrence of fatal electrical instability of the myocardium.

The description of an autopsy case with chronic total hypothermia provides the rare opportunity for experimental results to be confirmed in humans and is also an original contribution.

The scientific and applied aspects arise from the possibilities of molecular-pathological studies to determine appropriate targets for therapeutic intervention and/or factors with predictive and/or prognostic value. Such facts are:

- the creation of algorithms for the morphological assessment of salivary gland tumors

- the study of cytokeratin expression in glioblastoma multiforme, for the correct determination of the histogenesis of the tumor
- the frequency and distribution of histologically confirmed intracranial tumors and the study of a large number of histologically proven cases of head and neck tumors have an original contribution to the Bulgarian population
- the description of histological changes in the lungs in COVID-19 in humans is relatively insufficient on a global scale

A significant share in the scientific activity of Dr. Stoeva is occupied by descriptions of cases from the practice of the pathologist. The description of cases contributes to the enrichment of the scientific literature on rare diseases and improves their diagnosis.

CONCLUSION

The documentation submitted for the Competition is in full volume and meets the procedural requirements in the regulatory documents. The candidate's scientific production corresponds to the necessary criteria. I am impressed by the personal and professional qualities of the candidate and I believe that she fully meets the conditions for holding the position. Based on the acquaintance with the presented scientific works, their significance, the scientific and scientific-applied contributions contained in them, I find it reasonable to propose Dr. Martina Stoeva to occupy the academic position of "Associate Professor" in the professional field 7.1. Medicine, area 7. Health and sports and I vote positively for this with full conviction.

20.02.2025

Varna

Signature:

(Prof. Peter Ghenev, MD, PhD)

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