

# STATEMENT

by

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Member of the Scientific Jury according to Order P-109-96/21.03.2024

of the Rector of Medical University of Varna,

**Regarding:** Competition for the academic position of „ **Full Professor**” in the field of higher education **4. „Natural sciences, mathematics and informatics”**; professional direction направление **4.3. „Biological Sciences”** and scientific speciality **“Biochemistry”**, for the needs of the "Biochemistry, Molecular Medicine and Nutrigenomics" Department, Faculty of Pharmacy, MU-Varna with additional conditions for the competition: candidates must have acquired a specialty in biochemistry. The competition was announced in the 07/23.1.2024 issue of the "State Gazette".

The members of the scientific jury, appointed by order of the Rector of MU-Varna R-109-96/21.03.2024, after evaluating the candidate's scientific output, found that it corresponds to the minimum national requirements under Art. 2b, paragraph 2 and paragraph 3 of the Law on the Development of the Academic Staff in the Republic of Bulgaria and allow the only candidate to participate in the competition, Associate Professor Maria Atanasova Radanova, PhD.

## **I. BIOGRAPHICAL DATA AND PROFESSIONAL DEVELOPMENT**

Maria Atanasova Radanova was born on May 14, 1975 in Ruse. She completed her higher education in 1999 with a master's degree in "Molecular Biology", specialization "Clinical Chemistry", Faculty of Biology, Sofia University "St. Kliment Ohridski", Sofia. Since 2007, she has been a PhD student at the Department of Biochemistry, Molecular Medicine and Nutrigenomics, specialty "Biochemistry", Medical University "Prof. Dr. Paraskev Stoyanov", Varna. She defended her thesis in 2012 on the topic "Study of molecular effects of C1q inhibition in patients with lupus nephritis", and in 2015 acquired a medical specialty "Biochemistry" from the University of Varna.

In 2000, she started working as a biologist at the Bulgarian Academy of Sciences, Institute of Reproductive Biology and Immunology "Acad. Kiril Bratanov", Sofia, and between 2001 and 2006 she worked as a biologist, assistant, and senior assistant at Ruse University "Angel Kanchev", branch - Silistra. From December 2006 until now, she has been working at the Medical University "Prof. Dr. Paraskev Stoyanov", Varna, Department of "Biochemistry, Molecular Medicine and Nutrigenomics", passing through all stages of career development as an assistant prof., senior assistant prof, chief. assistant prof. From 2016 to the present, she is an associate professor, specialty "Molecular Biology", Department of Biochemistry, Molecular Medicine and Nutrigenomics, Medical University "Prof. Dr. Paraskev Stoyanov", Varna. She works in the Laboratory of Molecular Pathology at the UMBAL "St. Marina", Varna in the period from 2017 to 2023. Currently, from the beginning of 2024, she is an established researcher (R3) in scientific group 3.1.1. on the project: "Medical University - Varna: Increasing Translational Achievements in Medicine (MUVE-TEAM)", Research Institute at the Medical University "Prof. Dr. Paraskev Stoyanov", Varna.

During the period 2019-2023, Assoc. Prof. Radanova also participated in numerous postgraduate online lecture and practical courses.

## **II. General assessment of research activity**

### **1. Summary characteristics of scientific production and publication activity**

The total number of publications of Assoc. Prof. Radanova, with which she participates in the current competition, are:

- The dissertation work for obtaining the educational and scientific degree "Doctor";
- 5 scientific publications that are referenced and indexed in world- renowned databases with scientific information (Web of Science and Scopus), equivalent to a habilitation thesis.
- 9 scientific publications, in editions that are referenced and indexed in world-renowned databases with scientific information (Web of Science and Scopus), beyond those equivalents to habilitation work
- 2 published book chapters
- 1 chapter in a published university textbook
- 2 published university textbooks, of which she is scientific editor.

Prof. Radanova is the corresponding and/or first author in 7 of the 16 scientific papers provided, and in 5 of them he is the last author. In addition, 2 full-text publications in scientific publications, referenced and indexed in global databases with scientific information, are presented, beyond the minimum scientometric requirements for occupying AD "professor". The journals in which Assoc Prof. Radanova publishes have a total IF of 44,892 and a total Scimago Journal Rank of 10,732.

According to the provided reference, the total number of citations of Prof. Radanova's works is 119 in Web of Science and Scopus. Prof. Radanova presented for the period 2019-2023 11 participations in international and 3 in national scientific forums, with poster presentations and reports in 3 of the forums.

### **2. Assessment of research activity and contributions**

The research activity of Prof. Radanova in the Department of Biochemistry, Molecular Medicine and Nutrigenomics has been going on for over 18 years. Her main scientific interests and achievements during these years are related to the study of diagnostic, prognostic and predictive biomarkers in solid tumors. Among them, the candidate's special interest in non-coding RNAs (ncRNAs) and single nucleotide polymorphisms (SNPs) stands out, as well as in various protein and genetic biomarkers with prognostic and predictive significance.

Another area of special interest is the study in patients with autoimmune diseases of the molecular effects of inhibition of C1q – the first component of the complement system. Prof. Radanova also works in the field of pathological dysregulation of metabolism.

The original and innovative contributions of the scientific works included for participation in the competition are grouped in this report into three categories - of a scientific theoretical nature, of a scientifically applied nature and of a methodological nature, and are presented according to the scientific directions described above.

Undoubtedly, the most significant scientific contributions have been the publications in recent years, equivalent to habilitation work, in the field of non-coding RNA and SNP variants in them, in patients with colorectal carcinoma. The aim of the research of

interdisciplinary teams under the leadership of Associate Professor Radanova within two research projects and one doctoral dissertation was to identify new diagnostic, prognostic and predictive biomarkers.

Original scientific contributions in this subfield of a scientific-theoretical nature are the creation of a database of circular RNAs (circRNAs) with an oncogenic function in colorectal carcinoma. An original interpretation of the mechanisms by which transcribed-ultraconserved regions (T-UCRs) regulate gene expression is also presented, as well as the mechanisms by which the expression of T-UCRs themselves is regulated.

Scientific-applied contributions are related to the identification of two new circulating circRNAs for colorectal carcinoma, which distinguish patients in stage IV from patients in stage III of the disease. The prognostic potential of mir-618 in patients with advanced disease has been established. Single nucleotide polymorphisms (SNPs) in miRNA genes have been found to be associated with the prognosis of patients with metastatic colorectal cancer and with the risk of developing the disease, and these associations are not mediated by the levels of the respective miRNAs. A methodical contribution is elucidating the role of miRNAs in liver metastasis in colorectal carcinoma within a specialized textbook for surgeons.

The other important area of research is more clinically oriented, related to proving the predictive and prognostic role of various markers in metastatic colon cancer, such as establishing the relationship between RIPK3 expression levels in the primary tumor and the aggressiveness of the disease. The frequency of KRAS mutations in Bulgarian patients with advanced and metastatic colorectal carcinoma was also determined.

For the first time, NSCLC patients with high NLR (neutrophil/lymphocyte ratio) and sarcopenia who progressed on platinum-based chemotherapy were shown to be at higher risk of developing hyperprogressive disease after immunotherapy as a treatment for second line. In Bulgarian patients with metastatic breast cancer (HR+/HER2-), the frequency of PIK3CA mutations was determined and it was found that the presence of the mutation did not affect the response to endocrine therapy as a first-line treatment.

The scientific direction for the study of the molecular effects of the inhibition of C1q - the first component of the complement system in patients with autoimmune diseases is based on the dissertation of Assoc. Radanova and is being upgraded with new studies, within the framework of an international research project and a doctoral dissertation under her supervision guide. An original contribution was the discovery of a functional deficiency of C1q, which indicated the critical role of regions located in the collagen stalk region of the protein in maintaining tolerance to self-structures.

The functional consequences of the binding of autoantibodies and hemolysis products to the globular domains of C1q have been established, which could explain the insufficient clearance of immune complexes and CRP-opsonized apoptotic cells in lupus nephritis.

A scientifically applied contribution is the establishment of an association of SNPs located in the C1q gene cluster with the risk of developing rheumatoid arthritis in a Bulgarian cohort.

Prof. Radanova is involved as an expert in the research related to the study of "Pathological Dysregulation of Metabolism" within the framework of wider collaborative projects. Contributions of a scientifically applied nature are reported here. A cytoprotective effect on hepatocytes of S-adenosylmethionine was established by increasing the expression of the heme oxygenase-1 enzyme in conditions of fructose-induced disorder.

Serum levels of SC-18 (cytokeratin-18) have been found to correlate with histological and biochemical changes in liver damage and can be used as a biomarker for non-invasive assessment of its progression in metabolic syndrome. The first meta-analysis evaluating the association between variants in dynein-related genes and male infertility was conducted.

### **III. Participation in and leadership of scientific projects**

Prof. Radanova participated in the implementation of 3 projects financed by the National Science Fund, Ministry of Education and Science (3), one of which is in line with bilateral cooperation with France. She is the leader of two and a participant and work package leader in 1 project. Prof. Radanova participated in 6 projects financed by the "Science" Fund of MU-Varna, managing 2 of them.

Prof. Radanova is currently an established researcher (R3) in scientific group 3.1.1. on the project: "Medical University - Varna: Increasing Translational Achievements in Medicine (MUVE-TEAM)", Research Institute at the Medical University "Prof. Dr. Paraskev Stoyanov", city of Varna, financed by NPVU.

### **IV. Scientific Supervision of PhD students**

Prof. Radanova is the supervisor of 1 doctoral student in the "biochemistry" doctoral program and co-supervisor of two doctoral students in the "Internal Diseases" and "Oncology" doctoral programs, and all three have successfully defended their dissertations.

### **V. Assessment of academic workload**

The submitted study load report shows that Associate Professor Radanova is a teacher with an extremely high level of commitment in the teaching and learning activities of the Department of Biochemistry, Molecular Medicine and Nutrigenomics of the University of Varna. It can be seen from the provided reference for the last 5 years that the study load with lectures and exercises far exceeds the required norm. Her educational workload also includes teaching biochemistry, clinical laboratory and biochemistry, clinical laboratory, biochemistry and immunology to students majoring in kinesitherapy, nursing and midwifery, medical assistant from the Faculty of Public Health and Health Care, Angel Kanchev University of Ruse.

### **Conclusion**

From the general characteristics of the candidate, Assoc. Radanova, it can be concluded that she has established herself as an excellent teacher, supervisor, university scientist and specialist in the field of biochemistry and molecular biology. It should be noted the persistence and purposefulness with which she develops her scientific activity, as well as her thorough and systematic approach, dedication and commitment to her teaching work. Assoc. Prof. Maria Radanova fully fulfills, exceeding the minimum national requirements and the requirements of MU – Varna in the field of the announced competition for awarding the scientific title "Professor".

Based on this, I strongly recommend the Scientific Jury to vote "YES" for the awarding of the academic position "Professor" to Assoc. Maria Radanova.

27.05.2024

Sofia

**Signature:**

Заличено на основание чл. 5,  
§1, б. „Б“ от Регламент (ЕС)  
2016/679

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