ATTN: THE CHAIRMAN OF THE SCIENTIFIC JURY ANNOUNCED BY ORDER NO R-109-96/MARCH 21, 2024 OF THE RECTOR OF THE MEDICAL UNIVERSITY 'PROF. PARASKEV STOYANOV' OF VARNA

STANDPOINT

by Assoc. Prof. Galina Alexieva Yaneva, PhD
Head, Department of Biology, Faculty of Pharmacy at Medical University 'Prof. Paraskev Stoyanov' of Varna

Concerning: the competition for the academic position of '**Professor**' in the field of higher education No 4 Natural sciences, mathematics and informatics, professional trend No 4.3 Biological sciences and speciality of Biochemistry at the Faculty of Pharmacy, Department of Biochemistry, Molecular Medicine and Nutrigenomics at the Medical University 'Prof. Paraskev Stoyanov' of Varna according to Order of the Rector, Prof. Dimitar Ivanov Raykov, MD, PhD, DSc, promulgated in State gazette No 7/January 23, 2024.

According to Order No R-109-96/March 21, 2024 of the Rector of the Medical University 'Prof. Paraskev Stoyanov' of Varna and by Protocol No 1 of the Scientific jury, I was elected internal member of the jury in a procedure for tenure of the academic position of '**Professor**' in the Medical University 'Prof. Paraskev Stoyanov' of Varna and I am assigned for standpoint preparation concerning the competition. Assoc. Prof. Maria Atanasova Radanova, PhD, is the only candidate.

The documents submitted to me conform with the Law for development of the academic staff in the Republic of Bulgaria and the Statute-book for its application and meet the requirements of the Statute-book for the conditions and order for the acquisition of scientific degrees and for tenure of academic positions in the Medical University 'Prof. Paraskev Stoyanov' of Varna. No procedural infringements were established.

I declare that I have no conflict of interest in the sense of article 4, paragraph 5 of the Law for development of the academic staff in the Republic of Bulgaria.

I. CONCISE BIOGRAPHICAL DATA AND CAREER DEVELOPMENT

Maria Atanasova Radanova was born on May 14, 1975 in the city of Rouse. She graduated from St. Kliment Ohridski University of Sofia in 1999 as master in the speciality of Molecular biology. Maria Radanova started to work as a biologist in the Institute of Biology and Immunology of Reproduction 'Academician Kiril Bratanov' of the Bulgarian Academy of Sciences on February 21, 2000, where she worked until December 29, 2000. During the period between October 22, 2001 and December 1, 2006, she worked as a biologist, assistant and senior assistant in the Branch of the University 'Angel Kanchev' of Rouse. Then until the present moment, she consecutively worked as assistant, senior assistant and assistant-in-chief

in the Department of Biochemistry, Molecular Medicine and Nutrigenomics at the Medical University 'Prof. Paraskev Stoyanov' of Varna. During the period between 2007 and 2011, she was doctoral student in independent preparation form at Department of Biochemistry, Molecular Medicine and Nutrigenomics in the speciality of biochemistry in the Medical University 'Prof. Paraskev Stoyanov' of Varna. In 2012, she successfully defended a dissertation for the acquisition of the educational and scientific degree of 'doctor of philosophy' on the theme of 'Investigation of molecular effects due to C1q inhibition in lupus nephritis patients'. She attained academic rank of associate professor in the scientific speciality of Molecular biology in 2016. Until January 1, 2023, she is associate professor in the Laboratory of Molecular Pathology at St. Marina University Hospital of Varna. Since the academic year 2011-2012 until presence, she is a part-time lecturer in the Faculty of Public Health and Nursing Care of the University 'Angel Kanchev' of Rouse. Since February 20, 2024 until presence, she is established researcher in the scientific group 3.1.1 within the project: 'Medical University of Varna: Enhancement of the translational achievements in medicine (MUVE-TEAM) of the Research Institute of the Medical University 'Prof. Paraskev Stoyanov' of Varna'.

II. RESEARCH ACTIVITY

Assoc. Prof. Maria Atanasova Radanova, PhD, participates in the present competition with the following scientific works:

- a dissertation work for the acquisition of the educational and scientific degree of '**doctor of philosophy**';
- five scientific publications in editions which are abstracted and indexed in world-famous data-bases with scientific information (*Scopus* and *Web of Science*) equal in value to a research work qualifying for an academic degree;
- nine scientific publications in editions which are abstracted and indexed in world-famous data-bases with scientific information (*Scopus* and *Web of Science*) beyond the equivalent ones to a research work qualifying for an academic degree;
- two published book chapters;
- one chapter in a published university textbook of a total volume of 16 pages;
- two published university manuals of a total volume of 247 pages as in one of them she is scientific editor, and
- two full-text articles in scientific editions abstracted and indexed in world-famous data-bases with scientific information beyond the minimal scientometric requirements for tenure of the academic position of '**Professor**'.

The journals in which the scientific works have been published during the period between 2017 and 2023 present with a total Impact Factor of 44,892 and a total of Scimago Journal Rank of 10,732.

A total of eight publications have been cited a total of 119 times in scientific editions, monographs and collective volumes, and patents abstracted and indexed in world-famous data-bases with scientific information (*Scopus* and *Web of Science*).

Moreover Assoc. Prof. Maria Atanasova Radanova, PhD, submits a list with three participations in scientific forums in Bulgaria and with 11 participations in scientific forums abroad during the period between 2019 and 2023.

Assoc. Prof. Maria Atanasova Radanova, PhD, is adviser of three doctoral students who have successfully defended their dissertation works. She is participant in four research or educational projects in Bulgaria, head of three research or educational projects in Bulgaria, and head of the Bulgarian team in one international research or educational project.

The publications submitted by Assoc. Prof. Maria Atanasova Radanova, PhD, for participation in the competition completely correspond to the recommended quantitative criteria for tenure of the academic position of '**Professor**' in the Medical University 'Prof. Paraskev Stoyanov' of Varna according to the Statute-book for the conditions and order for the acquisition of scientific degrees and for tenure of academic positions in the University.

III. CHARACTERISTICS AND CONTRIBUTIONS OF THE SCIENTIFIC PUBLICATIONS

The research activity of Assoc. Prof. Maria Atanasova Radanova, PhD, is devoted to a series of particularly topical and socially significant interdisciplinary problems.

The main scientific directions of the scientific works submitted by her are three:

i) Diagnostic, prognostic and predictive biomarkers in solid tumours with two subdirections:

a) diagnostic and prognostic role of some biomarkers such as non-coding ribonucleic acids and single nucleotide polymorphisms in their genes (presented in seven articles: B4.1-B4.5, Г8.2, and E19) and b) prognostic significance of some protein and genetic biomarkers (presented in four articles: Г7.1- Г7.4).

ii) Molecular effects due to the inhibition of C1q, the first component of the complement system, in patients with autoimmune diseases (presented in the dissertation work - A1 and in three articles: Г7.8, Г7.9, and Г8.1).

iii) Disturbed regulation of the metabolism (presented in five articles: Г7.5-Г7.7 and two articles beyond the minimal requirements).

The main original scientific contributions of these publications are characterized as scientific and theoretical, scientific and applied, and methodical.

The scientific and theoretical contributions of the publications in the subdirection of 'Diagnostic and prognostic role of some biomarkers such as non-coding ribonucleic acids and single nucleotide polymorphisms in their genes' are the following:

1. A data-base of the circular ribonucleic acids with oncogenic function in colorectal cancer with detailed information about all the known nominations of the corresponding circular ribonucleic acid, about the mechanism of its action, about the established associations with the clinical and pathological features of the disease and about its potential as a diagnostic and/or prognostic biomarker has been created (B4.1).

2. An original interpretation of the mechanisms through which the transcribed ultraconserved regions regulate the gene expression and of the mechanisms of regulation of the expression of these regions has been presented (Г8.2).

The scientific and applied contributions of the publications in this subdirection are the following:

1. For the first time, two new circular ribonucleic acids in colorectal carcinoma through which the patients at stage IV are distinguished from those at stage III of the disease

have been established. One of them has a prognostic significance in metastatic carcinoma patients (B4.2).

2. For the first time, the prognostic potential of one microribonucleic acid in the patients with advanced colon carcinoma has been established (B4.3).

3. Single nucleotide polymorphisms in the genes of the microribonucleic acids related to the prognosis of metastatic colorectal cancer patients and to the risk of disease development have been established. These associations are not mediated by the levels of the corresponding microribonucleic acids (B4.3 and B4.4).

The methodical contribution of the publication in this subdirection is the following:

1. New data about the biology of colorectal carcinoma liver metastases have been generalized and the role of the microribonucleic acids in a specialized textbook of surgery has been outlined (E19).

The scientific and applied contributions of the interdisciplinary publications in the subdirection 'Prognostic significance of some protein and genetic biomarkers' devoted to the colorectal carcinoma, non-small-cell lung cancer and metastatic breast cancer are the following:

1. For the first time, the predictive and prognostic role of the receptor-interacting protein kinase 3 (RIPK3) in the metastatic colon cancer and the relationship between its expression levels in the primary tumour, on the one hand, and disease aggressiveness, on the other hand, has been evaluated (Г7.1).

2. For the first time, the frequency of the mutations in KRAS gene in Bulgarian patients with advanced and metastatic colorectal cancer has been evaluated (Г7.2).

3. It has been proved for the first time that the patients with non-small-cell lung cancer and with a high neutrophil : leukocyte ratio and sarcopenia in whom the disease progresses following first-line platinum chemotherapy are exposed to a higher risk of hyperprogressive disease after the immunotherapy as a second-line treatment (Г7.3).

4. For the first time, the incidence of PIK3CA mutations in Bulgarian female patients with metastatic breast cancer (HR+/HER2-) has been studied, and it has been established that mutation presence does not affect the response to the endocrine therapy as a first-line treatment (Г7.4).

The scientific and theoretical contributions of the publications in the direction of 'Molecular effects due to the inhibition of C1q, the first component of the complement system, in patients with autoimmune diseases' are the following:

1. For the first time, a functional C1q deficit has been detected which demonstrates the crucial role of the functional sections located in the area of collagen stems of the protein for the maintenance of the tolerance towards the own structures (A1).

2. The functional consequences from the binding of the autoantibodies and haemolysis derivatives with C1q globular sections that could explain the insufficient clearance of the immune complexes and apoptotic cells opsonized through C-reactive protein in lupus nephritis have been established (A1).

The scientific and applied contribution of the publication in this direction is the following:

1. In a Bulgarian cohort, an association between several single nucleotide polymorphisms with a linkage disequilibrium located in C1q gene cluster, on the one hand,

and the risk of rheumatoid arthritis, on the other hand, has been established. This relationship has not been predetermined by C1q plasma levels (Г7.9).

The methodical contributions of the publications in this direction are the following:

1. The mere theme about the role of the complement system in the pathogenesis of rheumatoid arthritis among Bulgarian rheumatologists has been popularized through a publication in the journal '*Rheumatology*' (Г7.8).

2. A detailed protocol for routine detection of anti-C3 antibodies in plasma through ELISA method has been presented (Г8.1).

The scientific and applied contributions of the publications in the direction 'Disturbed regulation of the metabolism' are the following:

1. The cytoprotective effect on hepatocytes of S-adenosylmethionine through enhancement of the expression of the enzyme heme oxygenase-1 under the conditions of fructose-induced disorder has been established (Г7.5).

2. It has been established that serum cytokeratin-18 levels correspond to the histological and biochemical alterations in liver damage and they can be used as a biomarker for the noninvasive assessment of its progression in metabolic syndrome (Г7.6).

3. For the first time, a meta-analysis of the association between the variants of dynein-related genes and male infertility has been carried out. For the first time, the pathogenic variants in these genes have been distinguished from their harmless variants. Besides for the first time, these genes as molecular targets for future investigations on the problems of sperm mobility have been described (Г7.7).

The generalization can be drawn that the number of the original contributions in the publications of Assoc. Prof. Maria Atanasova Radanova, PhD, submitted for tenure of the academic position of **'Professor'** is considerable: a total of 18, of which four are scientific and theoretical, 11 are scientific and applied, and three are methodical.

IV. TEACHING AND LECTURER'S ACTIVITY

Assoc. Prof. Maria Atanasova Radanova, PhD, is involved in the Bulgarian language and in the English language education of students. Her teaching and lecturer's activity as associate professor in the Department of Biochemistry, Molecular Medicine and Nutrigenomics during the period between 2019 and 2023 is the following: during the 2019-2020 academic year - 42 hours of lectures and 87 hours of exercises in the Bulgarian language and three hours of lectures in the English language education; during the 2020-2021 academic year - 55 hours of lectures and 185 hours of exercises in the Bulgarian language education; during the 2021-2022 academic year - 89 hours of lectures and 110 hours of exercises in the Bulgarian language education, and during the 2022-2023 academic year - 123 hours of lectures and 174 hours of exercises in the Bulgarian language education.

CONCLUSION

Based on candidate's scientific works submitted for peer reviewing and analysis, I can entirely convincingly declare that I vote positively for the election of Assoc. Prof. Maria Atanasova Radanova, PhD, for tenure of the academic position of **'Professor'** in the scientific speciality of 'Biochemistry' in the Department of Biochemistry, Molecular Medicine and

Nutrigenomics, Faculty of Pharmacy at the Medical University 'Prof. Paraskev Stoyanov' of Varna.

May 21, 2024

(*Assoc. Prof. Galina Alexieva Yaneva, PhD*)