To:
The chairman of the scientific jury,
according to Order No. R-109-144/23.02.2023. of the Rector of MU - Varna
55 Marin Drinov St., Varna 9002

Attached I present:
REVIEW
by Competition for the academic position "Professor"
Scientific specialty "Hematology and blood transfusion", Area of Higher Education 7. "Health care and sports", professional direction 7.1 "Medicine"
Announced in State Gazette, issue 102/23.12.2022 for the needs of MU-Varna, Second Department of Internal Medicine

Reviewer: Prof. Zhanet Grudeva-Popova, MD, PhD, MHM
Specialties: Internal Medicine, Clinical Hematology, Medical Oncology
Institutions: MU-Plovdiv, Deputy Dean for Research, Faculty of Medicine, Head of the Department of Clinical oncology
Head of Clinical Hematology Clinic - UMBAL "Sv. Georgi" EAD, Plovdiv

Address and contacts:
UMBAL "Sv. George" - EAD, Vasil Aprilov Blvd. No. 15A, 4002 Plovdiv
Email address: dr_grudeva@yahoo.com
Phone: +359 888 254 816; 032/ 602 777

REVIEW
COMPETITION FOR THE ACADEMIC POSITION OF "PROFESSOR" IN MU-VARNA

Assoc. Prof. Ilina Dimitrova Micheva, MD is the only candidate for participation in the announced (SG 102/23.12.2022) competition for the academic position of "Professor" in the scientific specialty "Hematology and Blood Transfusion" at the Second Department of Internal Medicine, Faculty of Medicine of MU-Varna. The procedure for announcing and conducting the competition is in accordance with the requirements of the Law on Academic Staff Development of Medical University of Varna, the Regulations for the Implementation of the Law on Academic Staff Development of Medical University of Varna, as well as the conditions for holding academic positions.
The submitted set of materials on paper/electronic media is in accordance with Article 137 of the Regulations for the Development of Academic Staff of MU-Varna.
I declare that there is no conflict of interest in the preparation of the review.
I have not found any plagiarism in the works submitted for review.

I. Analysis of the candidate's career profile
Assoc. Prof. Dr. Micheva, PhD was born in 1968 in the town of Isperih. She received her secondary education (1987) at the First Language School with English language studies - Varna. She graduated with honors from the Medical University of Varna (1993). She worked as a resident doctor (1994) at the Medical University of Varna, and in the period 1994-1998 she was specializing internal medicine at the same institution. She acquired a specialty in internal medicine (1998). Since 2000 is a full-time PhD student at the Department of Hematology - University of Patras, Greece with a scholarship from the Hellenic Foundation

for State Scholarships (IKY). She defended her thesis on "The role of dendritic cells in the hematopoietic defects in patients with myelodysplastic syndrome" (2005). In the period 2000-2005 she worked in the Scientific Laboratory in the same unit, where she mastered methods of cell and molecular biology; she participated in the team of research projects related to hematology, immunology, dendritic cells, cell and gene therapies; she applied the fluorescence activated cell separation system (FACSvantage, BD).
Assoc. Prof. Micheva started working in the Clinic of Clinical Hematology at the University Hospital "Sv. Marina", Varna (2006) and in the same year she acquired a specialty in clinical hematology. She is Head of the Department of Hematopoietic Stem Cell Transplantation (HSCT) at the clinic of the same name (2014-2022) and Head of the Clinic of Clinical Hematology from 2019 to present. Since 2008, she has been successively Assistant Professor, Senior Assistant Professor and Associate Professor at the Department of Internal Medicine (Department of Hematology), and since 2020 she has been Head of the Educational sector of Hematology at the Second Department of Internal Medicine.
In her professional field, Assoc. Prof. Micheva conducts individual trainings in the field of myeloid and lymphoid neoplasias, HSCT (specializations in Hanover, Ljubljana, SBALHZ - Sofia). She obtained her professional qualification in the highly specialized activity "Stem cell transplantation" at MU-Varna (2016). The main scientific interests and contributions of Assoc. Prof. Micheva are in the field of MDS, MPN, acute leukemias and HSCT.

II. Evaluation of the candidate's research activity
Assoc. Prof. Ilina Micheva submits for participation in the competition for the position of "Professor" a list of 97 scientific works for the period after habilitation as Associate Professor. The list includes 43 full-text publications (including two posters published in EHA e-library), 45 scientific communications and reports with printed abstracts at international and national scientific forums, 9 participations with reports at international and national scientific forums, co-authorship in one textbook on clinical hematology. Dr.Micheva is first author in 19, second author in 32, last author in 22 and consecutive author in 24 publications.
All the works of Assoc. Prof. Ilina Micheva in her professional scientific development have been cited 273 times, have a total impact factor of 302,462 and h-index -7.

SCIENTIFIC INDICATORS presented for the position "Professor" from the submitted academic reference

GROUP A: Dissertation for the award of PhD on "The role of dendritic cells in the hemayopoietic defect in patients with myelodisplastic syndrome", Medical University, Patras, Greece, (№1809-BAK, Sofia, 07.11.2007. (50 pts.).
GROUP OF INDICATORS B: Scientific publications in scientific journals, refereed and indexed in international databases with scientific information (Scopus and Web of Science), equivalent to a habilitation thesis -10 pcs. (156,02t)
INDICATOR GROUP G: Publications and reports published in scientific journals, refereed and indexed in international databases of scientific information (Scopus and Web of Science) -11 pcs. (219,05t).
Publications and reports published in non-refereed peer-reviewed journals or edited collective volumes: 12 pcs (172,22 pts).

GROUP OF INDICATORS D - Total citations 188 (2635pts.)

GROUP OF INDICATORS E - (361.2pts.)

Assoc. Prof. Micheva submits an additional 17 full-text publications in scientific journals, beyond the minimum scientific metric requirements for the position of AD "Professor".
The submitted academic transcript shows that the minimum scientometric requirements for the position of Professor at MU-Varna are met.

The candidate's scientific career began with participation in a scientific project of the Scientific Research Fund at the Ministry of Health (1994). After obtaining the specialty "Internal Medicine" she continued as a full-time PhD student at the Medical University of Patras (2000-2005). During that period she mastered the principles of flow cytometry and fluorescence activated cell separation, the methods of cell and molecular biology. She has been involved in various projects resulting in publications in Clinical Immunology, British J of Haematology, Leukaemia Research, Gene Therapy, Haematologica, J of Cell Biochemistry, Blood Cells Molecules and Diseases. The results of these projects have been awarded with three first prizes at the Hellenic National Congress of Hematology, as well as the prestigious Akagathos Gutas Award of the Hellenic Society of Hematology.
Since 2006, the research interests of Assoc. Prof. Ilina Micheva have been focused on the biological and clinical aspects of myeloid and lymphoid neoplasias, and since 2015 on hematopoietic stem cell transplantation. The main scientific and clinical areas are in the field of myelodysplastic syndromes (MDS), myeloproliferative neoplasias (MPN), acute myeloid leukemia (AML), multiple myeloma (MM), HSCT, infectious complications in oncohematology and post-transplant period, lymphomas.

Myelodysplastic syndromes (MDS)
An analysis of cases with chronic myelomonocytic leukemia with assessment of prognosis, survival and risk of transformation into acute leukemia is presented for the first time in the country. The first large-scale study in our country was conducted on 219 patients with MDS - overall survival was assessed according to socio-demographic characteristics, FAB and WHO2016 criteria, the risk group according to IPSS, IPSS-R and WPSS. The role of the comorbidity index and the degree of "vulnerability" on the outcome of patients with MDS was analyzed. The Charlson comorbidity index, a comorbidity index specific for patients before HCT (HCT-comorbidity index)); the MDS-specific comorbidity index (MDS- CI); and the Adult Comorbidity Evaluation-27 (ACE-27) are reviewed. The role of epigenetic mechanisms, the role of microRNAs, and molecular genetic disorders in the pathogenesis of MDS are presented.

Myelofibrosis (MF)
The role of regulators of iron metabolism, hepcidin and inflamatory cytokines (IL-6, IL-8) in the pathogenesis of anemia syndrome in patients with MF was investigated and the results are presented in 10 publications. For the first time, the three-year experience of several centers in the treatment with Ruxolitinib of patients with primary MF is presented.

Acute leukaemia (AL)
For the first time in this country, an original approach to the treatment of a patient with Ph+ ALL and T315I mutation with inotuzumab and ponatinib followed by allogeneic HSCT and maintenance treatment with ponatinib is presented.
A retrospective study in newly diagnosed adult patients with AL and data from conventional cytogenetic analysis was performed.
A historical review of the use of L-asparaginase in the treatment of ALL is presented.
The first retrospective study to evaluate the efficacy of azacitidine treatment in patients with MDS and AML is presented.

The diagnostic potential of SNP-microarray, NGS, Sanger sequencing, multiplex ligation-dependent probe (MLPA), PCR for genetic-molecular testing in AML is discussed.

Multiple myeloma (MM)

A retrospective analysis summarizes the genetic profile of patients with newly diagnosed MM. Patients were evaluated by classical cytogenetics and FISH.

The pathogenetic mechanisms of myeloma-induced bone disease were investigated. Different signaling pathways such as RANKL/RANK/OPG, Notch and Wnt/β-Catenin signaling; the variety of chemokines, signaling and effector molecules such as DKK-1, sclerostin, periostin, activin A and transcription factors were examined. Serum levels of periostin, sRANKL, osteopontin, sclerostin and DKK-1 were evaluated in newly diagnosed MM patients.

Results are presented from the PORT study (NCT04412707), which aimed to compare the pharmacokinetics of melphalan after central and peripheral administration of melflufen and to assess the local tolerability of peripheral melflufen administration.

The role of 18F-FDG PET/CT in the diagnosis and staging of newly diagnosed MM patients was evaluated.

Experience with Bortezomib maintenance therapy in MM patients after achieving a complete response or a very good partial response is presented.

Infectious complications in oncohematology and posttransplantation period

The spectrum and antibiotic resistance of bacterial pathogens causing infectious complications in oncohematology and posttransplantation period were studied for the first time in the country for a six-year period (2015-2020) (clinical material of the Clinic of Hematology, University Hospital "Sveta Marina"-Varna). 2828 haemocultures were investigated and for the first time the production of slime in Staphylococcus spp. isolates associated with bacteraemia in patients after HSCT was evaluated. The clinical relevance of the Aspergillus Galactomannan antigen test in the diagnosis of invasive pulmonary aspergillosis in patients with oncohematological diseases, including post-transplantation, was also evaluated.

For the first time in the country, the species diversity of clinically relevant Staphylococcus spp. isolates obtained from hemocultures of patients with central venous catheter after HSCT was investigated: their susceptibility to a range of antimicrobial agents was tested. The spectrum of multidrug-resistant bacteria -intestinal colonizers was also investigated.

The in vitro activity of ceftazidime-avibact was analyzed against an extended spectrum of beta-lactamase-producing and carbapenem-resistant Gram(-) bacteria found in blood/faecal samples of transplant patients.

The species diversity and antimycotic drug resistance profile of Candida spp. isolates obtained from clinical specimens of post- HSCT patients were analyzed.

Hematopoietic stem cell transplantation (HSCT)

For the first time, the results of the administration of autologous HSCs in MM patients treated in the Transplantation Unit over a 6-year period are presented. The outcome after administration of haploidentical HSCT in a series of 11 patients was evaluated.

In an original study, the outcome of patients with refractory non-Hodgkin's lymphomas and Hodgkin's disease after autologous HSCT was evaluated.

The results of chemo-G-CSF peripheral stem cell mobilization protocols in 40 patients with lymphomas who received autologous HSCT were retrospectively analyzed. A complex case of successful desensitization in a patient with CML and donor-specific antibodies prior to haploidentical allogeneic HSCT is also presented.

Lymphoproliferative neoplasias

The advantage of 18F-FDG PET/CT in the diagnosis and follow-up of a patient with diffuse large B-cell lymphoma and multiple extranodal lesions was demonstrated.
A case of a 63-year-old female patient with severe myasthenia gravis, possibly associated with recurrence of CLL, treated with combined targeted and immunotherapy is presented.
In the first multicenter study in the country, the Bulgarian experience of Brentuximab Vedotin treatment of patients with refractoriness/relapse after HSCT for Hodgkin lymphoma was analyzed. The results showed an improvement in therapeutic response, prolongation of time to progression and increased overall survival.
VEGF expression levels were studied in 60 newly diagnosed patients with aggressive and indolent non-Hodgkin lymphomas (NHL), and significantly higher VEGF levels were found in patients compared to healthy controls, in indolent compared to aggressive lymphomas, and in high compared to normal LDH values.
For the first time in Bulgaria, the level of platelet-neutrophil complexes (PNC) in 88 patients with indolent and aggressive NHL and their relationship with clinical and laboratory indices was investigated. Significantly higher PNC levels were found in patients with NHL compared to healthy controls, and in aggressive versus indolent NHL.
A rare case of a young woman with Langerhans cell histiocytosis with multisystem involvement including bone, orbit, pulmonary system, and central nervous system is reported.
For the first time in Bulgaria, the efficacy and safety of treatment with TruximaTM in combination with chemotherapy has been evaluated in 51 patients with NHL and CLL.
Two reviews present the therapeutic potential of Polatuzumab vedotin and Obinutuzumab in the treatment of diffuse large B-cell and follicular NHL.

Other
Participation in an international team randomized phase 3 clinical trial comparing best supportive care plus luspatercept versus placebo in adult patients with transfusion-dependent β-thalassemia.
The possibility that bispecific antibodies (BsAbs) induce reactivation of existing tumor-specific T lymphocytes was investigated. In an experimental model, TCR-dependent interaction of blasts-T cells after in vitro incubation with bone marrow CD3xCD123 BsAbs was investigated in patients with OML.
The putative protective role of HLA-II alleles in the development of MPN was investigated by NGS typing in 139 JAK2V617F(+), 46 CALR exon 9(+) patients with MPN and 1083 healthy controls.
Over a 10-year period, 1554 bone marrow karyotypes performed on both children and adults with hematologic disorders were analyzed and three cases of unsuspected chromosomal abnormality were identified.
Experience with rare clinical cases of CLL, POEMS syndrome, Hodgkin's disease, etc. has been shared.

Participation in project implementation and management
Assoc. Prof. Ilina Micheva has participated in 17 research projects - eight completed and nine ongoing, 12 national (head in three of them), 5 international (main coordinator in one).
Their structure is as follows. The funding institutions of the projects are the Science Fund, MU-Varna(7), Ministry of Health (1), Research Fund(2), Bulgarian Medical Association (1), MU-Patra(1), EU(1), MU-Varna (1), Radboud University Medical Center, Nijmegen (1), Austrian AGMT Group (1).

Completed projects
Participation in national scientific or educational projects:

- Scientific approaches to complementary and alternative medicine (CAM)-concept, context, quality of life. Sponsor: the Science Fund MU-Varna (session 2020). 2022-2022.
- Creating a database of blood donors in the Republic of Bulgaria for markers of transmissible infections", 2020 (Ministry of Health). 2020-2022.
- Invasive bacterial infections in patients after autologous and allogeneic bone marrow transplantation: etiological spectrum and resistance to strategic beta-lactam and glycopeptide antibiotics (No. 19019). Sponsored by the Science Fund MU-Varna (Session 2019). 2019-2022.
- Clinical aspects of intercellular adhesions in pleural inflammation and tumor metastasis. Summary report of research project NNPC1547, developed under Funding Contract LC442/94 with the National Research Fund Ministry of Education, Science and Technology - 1994-1996.

Participation in international scientific or educational projects:
- AGMT Academic Project, in collaboration with Bulgaria: "MABTENANCE: An international, multicentre, randomised phase III trial of Rituximab as maintenance versus observation therapy in patients with CLL". The study was conducted at the Clinical Department of Hematology, Medical Center "Sv. Marina"-EAD Varna, together with the Austrian group AGMT. 2009-2019 https://clinicaltrials.gov/ct2/show/Pro
- A study of reactive oxygen species biological effects in the pathogenesis of myelodysplastic syndrome. Project of hematology Division (Research laboratoryIV-V), Department of internal medicine, Patras University Medical School, Patras, Greece and Hematology division. Department of Internal Medicine, Medical University, Varna, Bulgaria. Laboratory coordinator - 2007-2009.
- In vitro dendritic cell generation and peripheral dendritic cell subsets in patients treated with purine nucleoside analogues, NATO EAP.RIG 982938. Return fellow project- 2007-2010.

Leader of national scientific or educational projects:
- Primary, post-thrombocythemia, post-thrombocythemia MF - involvement of inflamatory cytokines (interleukin-6, interleukin-8) and regulators of iron metabolism (hepcidin) in the pathogenesis of anemia syndrome. Dr. Stella Dimitrova, a full-time PhD student at the Clinic of Hematology, supervised by Assoc. Prof. Dr. Ilina Micheva, PhD. Scientific Research Project for Young Doctors up to 35 years of age, postgraduate and doctoral students at the BMA. (Contract No. 5/29.08.2019). 2019-2021.

III. Evaluation of equivalent publications (10 in scientific journals, refereed and indexed in international databases of scientific information (Scopus and Web of science only)) submitted by the candidate for the "PROFESSOR" competition.

Assoc. Prof. Ilina Micheva participated in the competition with a Habilitation thesis in the form of 10 scientific publications only for the field of higher education 7, published in foreign and Bulgarian journals, refereed and indexed in Scopus and Web of Science. The scientific publications submitted in connection with the habilitation are thematically related to sections of clinical hematology (malignant blood diseases and HSCT). Many of them were developed by interdisciplinary teams with participation of specialists in genetics, microbiology, immunology, imaging.

The main areas of the presented scientific publications are related to infectious complications in patients with oncohematological diseases and after HSCT, MM, MF, ALL, chronic myelomonocytic leukemia, 18F-FDG PET/CT in diagnosis and monitoring of therapeutic response in oncohematology.

IV. Citation of the candidate's publications in national and foreign literature (publication image)

Recognition of the quality of the published scientific works of Assoc. Prof. Ilina Micheva is the significant number of citations. Evidence from the academic citation list prepared by the MU-Varna Library is attached.

The citations reflecting the scientific activity of the candidate in the post-habilitation period are a total of 188 - 165 in scientific publications, referenced and indexed in international databases with scientific information or in monographs/collective volumes, 7 in monographs and collective volumes with peer review, 16 in non-refereed peer-reviewed journals.

The total impact factor of the publications for participation in the contest is 212, 178.

V. Comprehensive qualitative evaluation of teaching and learning activities, including scientific supervision of students, doctoral students, postgraduate students

Assoc. Prof. Ilina Micheva, PhD has extensive experience as a lecturer since 2008. The presented reference for teaching workload shows that the candidate has the required teaching employment, exceeding significantly the norm of MU-Varna (average 206.5 hours of exercises and 29.5 hours of lectures per year). She teaches a lecture course of BEO and AEO to medical students - the fifth course of clinical hematology and exercises AEO. Participates in semester and state examination committees.

Former and current supervisor of graduate students in clinical hematology. Conducts a basic course in Clinical Hematology.

Scientific supervisor of ten PhD students, three of whom have successfully defended. Seven of the PhD theses are in the field 7.1.Medicine, Scientific specialty "Hematology and blood transfusion", and three in the field 4.3.Biological Sciences - one at the Department of Microbiology and Virology and two at the Department of Medical Genetics.

Assoc. Prof. Micheva is a co-author of a manual on diagnosis and treatment of hematological diseases and is on the editorial board of a textbook on surgery.

As head of the educational sector, Assoc. Prof. Micheva is responsible for the overall organization and implementation of the educational, teaching and scientific activities of the Hematology Clinic.

VI. Scientific achievements (scientific authority)

Assoc. Prof. Ilina Micheva, PhD is the Vice-Chairman of the Board of Bulgarian hematology association.

She is the Chairperson of the Scientific Group "MPN and MDS" and a member of the Working Group on HSCT.

Since 2019 she is a member of the Expert Council on Clinical Hematology at the Ministry of Health.

Assoc. Prof. Dr. Micheva is a reviewer in British J of Haematology, Scripta Medica, J of IMAB, Folia medica, Asian Haematology Research Journal, Turkish J of Haematology. Reviewer at MU-Plovdiv-projects and "Scientific Research" Fund of the Ministry of Health.

Reviewer of monograph. "Integrative medicine: History, ideological development, informed choice and smart investment in the future". Varna, MU-Varna, 2021.

Part of the editorial team of Schwartz Principles of Surgery. Ninth edition.

Member of the editorial board of the journal "Hematology" and "Pro medic".

"Programme Committee" expert to the European Commission, and expert to the "AML Community of excellence".

She is Head of the Blood and Blood Products Committee at the University Hospital "Sv. Marina"- Varna.

She is a member / chairman of scientific juries for the position of "Professor"(1), "Associate Professor" (2), "Senior Assistant Professor"(5) and for the acquisition of the degree of "Doctor"(5) at MU-Varna, MU-Pleven, MU-Plovdiv, MMA-Sofia.
The importance of Assoc. Prof. Micheva's research activity is also evidenced by the awards received: Akagatos Gutas" of the Hellenic Society of Hematology (2005), award of the Hellenic Society of Hematology for the best presentation (2002, 2003, 2005).
She has been awarded the title of "Doctor of the Year", field "Innovation" (2018 and 2019) by the BMA - Varna.
All of the above is in support of respect and professional authority based on valuable scientific and creative achievements.
VII. Critical comments and recommendations - none

VII. General assessment of the candidate's compliance with the minimum national requirements under Article 2b, paragraphs 2 and 3, respectively the requirements under Article 2b, paragraph 5 of the Law on Academic Staff Development in Republic of Bulgaria and the requirements specific to MU-Varna by areas of clinical activity, as defined in the Regulations for Academic Development at MU-Varna
Assoc. Prof. Ilina Micheva, MD, PhD fully meets and in many respects exceeds the criteria of the Law on Academic and Professional Development for the academic position of Professor. The candidate's scientific research and publication activity; her clinical and diagnostic activity in the field of clinical hematology; her responsible participation in the training of students, postgraduates and doctoral students; her contribution to the development of specialized staff in clinical hematology make her a respected and sought-after expert for participation as a consultant, reviewer, member of a scientific jury, participant in examination committees, scientific projects, etc. Knowing Assoc. Prof. Micheva personally and professionally, I am sincerely convinced of her potential for future development in the field of clinical hematology and HSCT.

IX. Conclusion
Assoc. Prof. Micheva, MD, PhD is an established specialist in the field of clinical hematology and HSCT, university teacher and scientist. The candidate meets the minimum national requirements under Article 2b, paragraphs 2 and 3, respectively the requirements under Article 2b, paragraph 5 of the Law on Academic Staff Development in Republic of Bulgaria and the requirements specific to MU-Varna in the areas of units with clinical activity, set out in the Regulations for Academic Development at MU-Varna for holding the position of "Professor".
In view of the above, **I strongly recommend** the esteemed Scientific Jury to propose to the MU-Varna Faculty Council **to award the academic position of "Professor"** to **Assoc. Prof. Ilina Dimitrova Micheva, MD, PhD.**

REVIEWER: Prof. Zhanet Grudeva-Popova, MD, PhD, MHM