PEER REVIEW

by Prof. Svetoslav Georgiev, MD, PhD Rector

of Medical University of Varna

Regarding: competition for holding the academic position "Professor" in the field of higher education: 7. Healthcare and sports, professional field: 7.1. Medicine, scientific specialty: Cardiology, for the needs of ES of Cardiology, First Department of Internal Medicine, Faculty of Medicine, Medical University of Varna and First Clinic of Cardiology, University Hospital St. Marina, Varna, published in SG 28/28.03.2023. Additional conditions: the requirement of Art. 137, paragraph 1, item 6, from the Regulations for the Development of Academic Staff of MUV are not to be applied and the sum of the points for indicator group E for the field of higher education: 7. Healthcare and sports is to be 100, without the requirement ≥ 80 points for indicator 14.

By decree of the Rector of the Medical University of Varna P-109-269/25.05.2023, I was appointed as a member of the Scientific Jury for the said competition, and by decision of the scientific jury Protocol No. 1 from 08.06.2023 for its chairman and competition reviewer.

One candidate submitted documents for the competition: Assoc. Prof. Mariya Negrinova Negreva, MD, PhD, DSc (later in document - MN).

I declare that I have no conflict of interest with the candidate.

I have received all necessary documents for writing the review from the Career Development Center of the Medical University of Varna (MUV). The are precisely described and arranged by the candidate. The review was prepared in accordance with the requirements of the Law for the Development of Academic Staff in Bulgaria, Regulations for its implementation, and the Regulations for the Development of Academic Staff (RDAS) of the MUV.

Brief biographical information about the applicant

MN was born on November 6th, 1981 in Vratsa. She graduated from the English High School in Varna in 2000. Then she graduated with a Master's degree in Medicine from the MUV in 2006. Since 2006 she has been working at the First Clinic of Cardiology as a resident (2006-2008), assistant physician (2008-2016) and associate professor of cardiology (2016 - present). She acquired a specialty in cardiology in 2013. She was successively awarded a Doctor degree (2015) and Doctor of Sciences in cardiology (2022). The candidate is fluent in English, French and German.

Research output

According to the documents submitted for the current competition, the overall research output of the candidate includes: 71 publications with a total impact factor of 79.913; doctoral dissertation with title: "Dynamics of oxidative stress in patients with paroxysmal atrial fibrillation" (2014); postdoctoral dissertation with title: "Early abnormalities in the coagulation and fibrinolytic system in paroxysmal atrial fibrillation" (2022); habilitation monograph: "Atrial fibrillation. Changes in cytokine response" (2016); habilitation monograph: "Platelets: fundamental and clinical projections" (2023); co-authorship in 1 textbook and 1 handbook. There is no evidence of plagiarism according to the plagiarism report done by the MUV Library. 51 publications were presented for "Doctor", "Associate Professor" and "Doctor of Sciences".

MN has participated in 72 scientific forums, presenting e list and evidence for 41. Of them, 17 are in European congresses with own results: 6 oral presentations and 11 posters. 12 of the participations in European congresses were published in journals referenced in WOS/Scopus.

For the current competition, MN's research output includes: 20 publications [14 in international (4 indexed in WOS/Scopus) and 6 in Bulgarian journals]; habilitation monograph: "Platelets - fundamental and clinical projections"; co-authorship in the textbook "Clinical Echocardiography" and the two dissertations described above. As seen from the presented Academic report, the research output exceeds the minimum quantitative scientometric requirements for holding the academic position (AP) "Professor" according to RDAS of MUV in all indicators, despite the recently acquired degree "Doctor of Sciences" and exclusion of a large part of the research output for the purposes of the competition:

- Indicators G5-G9: 202 pts (min requirement of 200 pts).
- Indicator G7: 135 pts (min of 80 pts).
- Indicators D10-D12: 680 pts (min of 100 pts).
- Indicators E13-E22: 116.67 pts (min of 100 pts).
- Full-text publications, excluded from the minimum scientometric requirements for holding AP "Professor": 116 pts.

Proof of the importance of the candidate's research output is the number of positive citations: a total of 60, most of them (37) are in publications, indexed in WOS/Scopus. The number of citations is evenly distributed over the years, which is proof of the candidate's research persistence.

Currently, MN is involved in two major scientific projects: "Research of the Application of New Mathematical Methods for the Analysis of Cardiac Data" together with researchers from the Institute of Robotics at the BAS; "Circulating Histone Proteins as Biomarkers of Disease (CHiP-BiD)".

I accept MN's scientific contributions report without observations. In a summarized form, the contributions in the following fields clearly stand out:

Contributions related to the study of coagulation and fibrinolytic indicators, as well as platelet activity, in patients with paroxysmal atrial fibrillation (Publication No. 1, 3 and 4, Indicator G7)

Direct and convincing evidence is presented for the development of early significant systemic hypercoagulability during short (≤24 hours) episodes of paroxysmal atrial fibrillation, incl. patients with a very low thromboembolic risk (CHA2DS2-VASc score = 0, regardless of sex). She also clearly outlines the need for: timely periprocedural anticoagulant therapy until complete restoration of the hemostasis profile in accordance with the hemorrhagic risk; earliest attempt to restore sinus rhythm (Publication No. 1 and 3, Indicator G7; Indicator E13).

An objective premise is given for the clinical search for effective anticoagulation by influencing the activity of FXI and FXII (Publication No. 1 and 3, Indicator G7; Indicator E13).

A good diagnostic possibility for identifying the occurrence of paroxysmal episodes of atrial fibrillation in the plasma activity of FVIII was established (Publication No. 1, indicator G7). The possibility of ischemic stroke prediction in these patients using

TF, FVIII and vitronectin plasma levels has been outlined (Publication No. 3, indicator G7).

Enhanced platelet activity in the same group of patients was demonstrated by elevated plasma levels of β -TG and TF-4 (Publication No. 4, indicator G7).

Contributions related to the study of application of mathematical methods for analysis of cardiac data (Publication No. 2, Indicator G7; Publication No. 5, Indicator G8)

Heart rate variability analysis from a Holter-ECG recording using the Poincaré plot method (SD1) and Detrended Fluctuation Analysis (α2 and αall) has been shown to have excellent diagnostic value for supraventricular extrasystoles (Publication No. 2, Indicator G7), as well as possibility of distinguishing patients with heart failure, which in clinical practice will improve diagnosis and early detection of diseases (Publication No. 5, Indicator G8).

Contributions related to the study of echocardiographic indicators and NT-proBNP serum levels in patients with an implanted dual-chamber pacemaker (DDDR) (Publication No. 1, Indicator G8)

Early left atrial remodeling after DDDR implantation (up to week 24) was demonstrated, with a significant increase in left atrial volume index and NT-proBNP serum levels.

Contributions related to the study of endodontic pathology in cardiovascular patients (Publication No. 6, Indicator G8)

A link between oral hygiene and risk characteristics of cardiovascular patients has been shown, which is the reason why these patients should be a priority for dentists in dental health prevention (Publication No. 6, Indicator G8).

Contributions related to assessment of hemodynamic characteristics at highnormal arterial pressure by impedance-cardiography and capillaroscopy (Publication No. 7, Indicator G8)

Evidence has been obtained to support the view that high-normal blood pressure individuals have more pronounced changes (compared to normal blood pressure) in the vessel wall at the macro- and micro level, which can be assessed using non-invasive methods (Publication No. 7, Indicator G8).

Contributions related to the study of neurological complications after open heart surgery (Publication No. 4, Indicator G8)

A difference was found in the nature and frequency of neurological complications after coronary artery bypass graft surgery and valve replacement surgery (Publication No. 4, Indicator G8). Differences in risk factors for neurological complications after coronary artery bypass graft surgery and valvular prosthesis surgery have been clarified (Publication No. 4, Indicator G8).

Contributions of the presented textbook "Clinical Echocardiography" (Indicator E21)

Representing the main direction in the clinical and expert activity of the candidate, it presents the possibilities of modern echocardiography for diagnosis, assessment and follow-up of cardiovascular diseases. The rich information is illustrated with numerous color illustrations.

Publications No. 2 and 3, Indicator G8, as well as the review articles from the list of full-text publications, excluded from the minimum scientometric requirements for holding AP "Professor" are a pivot point in candidate's research, as they represent a thorough and up-to-date analysis of the problems under consideration.

As recognition of candidate's research activity I can point out her role as a section editor of the MUV journal Scripta Scientifica Medica, her participation in the editorial boards of the journals: Thrombosis and Hemostasis: Research, Journal of Blood Ddisorders, Merit Research Journal of Medicine and Medical Sciences, as well as being a reviewer of the Clinical and Applied Thrombosis and Hemostasis journal.

Educational and teaching activity

MN educational and teaching activity started in 2008 as an Assistant Professor in cardiology at the ETS of Cardiology and Rheumatology at the Department of Internal Diseases of the MUV. In 2016, she was appointed as Associate Professor of cardiology at the same department. Since 2018, she is the head of the ES of Cardiology at the First Department of Internal Medicine of the MUV.

At the moment, MN teaches the following courses: Internal Diseases part I, 4th year medicine students (in English and Bulgarian) medicine; Internal Diseases, 2nd year rehabilitation students (in Bulgarian); Pharmacotherapy, 5th year pharmacy students (in Bulgarian); Internal Diseases, 3rd year physiotherapy students (in Bulgarian); Cardiology (elective course) for medical students.

The educational and teaching activities of the candidate also include practical and theoretical training of 6th year interns (in English and Bulgarian), as well as cardiology specialists at the Medical University of Varna. From the presented report on teaching workload, issued by the MUV, we can see that the candidate meets and exceeds the requirements for the annual work load for holding AP "Professor" according to RDAS of MUV.

MN is chairman of the examination committees for the Internal Diseases Part I 4th year (in Bulgarian and English) semester exam and Internal Diseases 6th year (in Bulgarian and English) state exam. MN is an examiner at the examination committee of the state examination for acquiring the specialties: Cardiology and General Medicine. She participates in the training in congenital heart defects echocardiography, expert level at the MUV and is an examiner at the examination committee for acquiring of this legal capacity.

Her complex work as a teacher and examiner of students, trainee doctors and specialists in cardiology and Head of ES of Cardiology is a good prerequisite for adequate and effective update of the cardiology curricula of all specialties at MUV. Evidence of her educational and teaching experience is her function as a person in charge of the accreditation of the Clinic for training in cardiology.

MN was a scientific consultant for one graduate (TU-Sofia, 2015) and currently supervises 4 doctoral students: 3 in cardiology, 1 in health care nanagement program.

The presented information indisputably shows development in MN's educational and teaching activities development and accumulated experience, which is of extreme importance for the academic development of every lecturer.

Therapeutic-diagnostic and expert activity

MN's work experience as a physician is over sixteen years, as can be seen from the certificate issued by University Hospital St. Marina, Varna (SMV). After graduating in 2006 from MUV, she started working at SMV, where she is still working to date.

She successively held the positions of physician, physician assistant professor specialist, physician assistant professor cardiologist and physician associate professor cardiologist.

Since 2013, the candidate has a recognized specialty in cardiology. In the same year, she acquired a professional qualification in echocardiography - fundamental level, and in 2017 - an expert level.

The candidate's therapeutic-diagnostic and expert activities are aimed at noninvasive diagnostics. She has completed numerous courses to increase her qualification, the most important of which are consecutive long-term specializations at the Universitätsklinikum Augsburg, Augsburg, Germany under the supervision of Prof. Ludwig von Scheidt and at the Ospedale Niguarda Ca' Granda, Milan, Italy.

She is a member of a number of established professional organizations: Bulgarian Society of Cardiology (DKB), Bulgarian Society of Cardiology, European Society of Cardiology (ESC), European Association for Cardiovascular Imaging (EACVI), European Association for Percutaneous Cardiovascular Intervention (EAPCI), etc.

Conclusion

MN has substantial scientific and research activity and individual characteristics of a refined researcher. Over the years, she has consistently developed her teaching and learning skills, naturally arising from accumulation of clinical experience and finding application in her academic development. She is a member of a number of scientific societies and journal editorial boards with proven medical value.

Her positive development in all academic areas meets the requirements of the Law for the Development of Academic Staff in Bulgaria, its Regulations, and RDAS of MUV for holding the AP "Professor" and allows me to give a positive assessment of the candidate and support the awarding of the AP "Professor" to Assoc. Prof. Mariya Negrinova Negreva, MD, PhD, DSc for the needs of the ES of Cardiology, First Department of Internal Medicine, Faculty of Medicine, Medical University of Varna and First Cardiology Clinic, University Hospital St. Marina, Varna.

Varna, July 12th 2023

Signature:

ignature: (Prof. Svetoslav Georgiev, MD, PhD)