

TO THE CHAIR PERSON OF THE SCIENTIFIC JURY
APPOINTED WITH ORDER
NO R -109-242/26.07.2019
OF THE RECTOR OF
MEDICAL UNIVERSITY “PROF. DR. P. STOYANOV”- VARNA

REVIEW

By Prof. Dr. Ivan Shterev Donev, Ph.D.

Medical Oncology clinic, MHAT Nadezhda, Sofia

REGARDING: Performing a call for the academic position “Associate Professor” in the sphere of higher education 7. Health care and sport; professional field 7.1 Medicine, “Internal diseases” specialty, code 03.01.46, for the needs of the Faculty of Medicine, Department of “Propedeutics of Internal Medicine”, and the Internal Diseases Clinic in “Sveta Marina” University Multiprofile Hospital for Active Treatment JSC – Varna.

Promulgated in the State Gazette, issue 43/31.05.2019.

Esteemed members of the Scientific Jury,

Pursuant to order R-109-242/26.07.2019 of the Rector of Medical University – Varna I have been appointed a reviewer on the procedure of appointing the academic position “Associate Professor” to the applicant Chief Assistant Dr. Yavor Kostadinov Kashlov, Ph.D.

This review has been prepared in conjunction with:

- The Law on the Development of the Academic Staff in the Republic of Bulgaria;
- the Rules of the application of The Law on the Development of the Academic Staff in the Republic of Bulgaria;
- the Rules on the development of the academic staff in MU – Varna and the specific requirements for the occupation of the academic position “Associate Professor.

In order to prepare the review I have been provided with a set of documents on paper and electronic media (including copies of all full text publications, summaries, and a monograph), which meet the requirements for participation in the call.

Biographic information on the applicant:

Dr. Yavor Kostadinov Kashlov graduated as a doctor in 2009 from Medical University – Varna, Medicine specialty. In 2011 he started specialization and doctoral studies in Propedeutics of Internal Diseases - “Sveta Marina” University Multiprofile hospital for Active Treatment JSC – Varna. He was appointed Adjunct Assistant in the same year; in 2013 he was appointed a regular Assistant. In 2017 he acquired Internal Diseases specialty. Dr. Kashlov has been Resident Medical Officer in Cardiology since 2017.

Dr. Kashlov is the author of 32 full text publications in Bulgaria and abroad; as a first author he has citations in prestigious international magazines. He presented results of his own research at the international congress BIT's 10th International Congress of Cardiology, in Rome, 2018. In 2017 Dr. Kashlov defended a doctoral thesis on “Biological markers of necrosis and necroptosis in cardiovascular diseases”. He was awarded the educational and scientific degree “Doctor” on the scientific specialty *Internal Diseases*.

Scientific research

32 scientific publications in Bulgarian and foreign scientific editions were submitted for review, with a total volume of 170 pages and one monograph of 244 pages. For the period of 2014 – 2019 Dr. Kashlov is a first author in 9 of the submitted publications. The overall personal impact factor exceeds by far the requirements for a similar competition – 26.32! The applicant has diverse scientific interests – in the sphere of Cardiology (13 publications), in the sphere of Interventional Medical Imaging (3 publications), in the sphere of Psycho – Oncology (3 publications), in the sphere of Medical Oncology and Radiation Therapy (11 publications), and in the sphere of Metabolic Risk (2).

The qualitative scientometric indicators meet the requirements of MU – Varna for holding the academic post “Associate Professor”, where scientific research is evaluated on the basis of real publications in scientific magazines, monographs,

Congress summaries, positive citations in Bulgarian and foreign scientific sources, scientific reviews, reports and summaries from national and international scientific events etc.

As Assistant and Chief Assistant in the “Propedeutics of Internal Diseases” Dr. Kashlov has serious workload regarding his teaching activity – over 170 hours per year from 2013 – 2019.

Scientific contributions of Dr. Kashlov’s thesis:

In his doctoral thesis, one of the goals which the applicant sets, is to analyse the predictive value of the expression of potential markers of necrosis and necroptosis in terms of myocardial infarction and heart failure.

Necroptosis is a newly reported type of cell form. Its role is not yet completely clarified, but it has a potential role in the pathogenesis of cardiovascular diseases. The research of the established key protein – RIPK3 – for this process and its tracing in dynamics is a potential marker for staging and making prognosis on cardiovascular diseases.

- For the first time in Bulgaria levels of serum markers are researched for necrosis and necroptosis in patients with cardiovascular diseases.
- For the first time in the world of clinic practice the potential role of necroptosis was proven as a new mechanism of cell death in patients with acute myocardial infarction with ST segment elevation after successful reperfusion.
- For the first time in the world the potential role of necroptosis is reported in ischemic – reperfusion injury when testing people with STEMI
- For the first time in the world there is data demonstrating the predicative value of the necroptosis marker – RIPK3 – for bad ejection fraction when dehospitalising patients with myocardial infarction with ST sediment elevation.

- For the first time in Bulgaria it was reported that patients who died after myocardial infarction, had higher serum levels of the necrosis marker - HMGB1.

Defining the blood levels of RIPK3 and HMGB1 in patients with myocardial infarction with ST segment elevation – before and after PCI, can be an object of additional research in view of confirming their potential role as biomarkers – separately or in combination for improving the prognosis in these patients.

Scientific contribution of the scientific publications:

- The first clinical article in Bulgarian medical literature which treats the importance of miRNA (micro RNA) in cardiovascular diseases (publication 1)
- For the first time in Bulgarian medical literature the link between necrosis, necroptosis and cardiovascular diseases is taken into consideration. This gives opportunity for a more in-depth analysis and the development of potentially new therapeutic and diagnostic methods in view of optimizing treatment of patients with cardiovascular diseases (3, 5).
- For the first time in Bulgarian medical literature a review is made on the potential role of ferroptosis in the pathogenesis of different cardiovascular diseases (27).
- For the first time in Bulgarian medical literature the link between autophagy and cardiovascular diseases (e.g. myocardial infarction and heart failure) has been reported. The mechanisms and the role of this type of cell death are listed in physiological and in pathological states (15).
- For the first time in accessible literature there is a report on the potential connection between the values of SUV max and the autophagy marker – Beclin-1 – in the primary tumour. The predictive value of SUV max in liver metastases is shown.
- For the first time in accessible literature the presence of new small molecules (micro RNA) is reported. Their concentration in the serum after completing adjuvant chemotherapy has the ability to recognize early relapse patients from patients without relapse of the disease. This is one of the few

articles in accessible literature which treats the same problem for the patients in the IInd and IIIrd stage and shows the superiority of these molecules over the standard marker which has been used up to now – CEA (7).

The monograph which has been submitted for review, presents a different and modern view on Pathophysiology, diagnosis and the future promising therapeutic strategies for the treatment of myocardial infarction, heart failure and cardio-toxicity. Modern guidelines are listed for determining, diagnosis and terminology of these diseases. Special attention is paid on the potential connection for the development of these diseases and types of cell death, among which the newly reported ones – necroptosis and ferroptosis. It is my opinion that this is a unique edition in its own right in our country, which contains the most contemporary information on the molecular genetic and patho-physiological peculiarities of the myocardial infarction and heart failure.

Conclusion

Dr. Yavor Kostadinov Kashlov is a doctor with 8 years of work experience and has proven to be a conscientious clinician and a thorough scientist, who can work in a multidisciplinary team and has scientific interests which he develops parallel with his clinical activity.

Dr. Kashlov has demonstrated skills of deep and convincing analysis of the well-known medical literary data and the results of his own research. The submitted scientific production is proof for his diverse interests in different spheres of Cardiology, Oncology, Molecular Biology and Internal Diseases.

In my opinion Dr. Yavor Kashlov meets the necessary requirements and criteria, as well as the qualitative scientometric indicators to hold the academic position of “Associate professor”, which are listed in the Rules for development of the academic staff of MU – Varna.

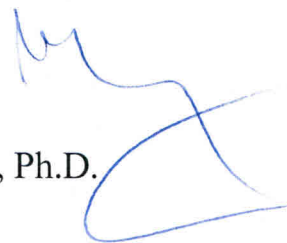
The comprehensive assessment of the scientific work which has been presented to me, is absolutely positive. This is why I suggest to the esteemed members of the Scientific Jury to vote positively on the choice of Dr Yavor Kostadinov Kashlov, PhD, for the position of “Associate Professor” on “Internal Diseases” for the needs of The Faculty of Medicine in the “Propedeutics of internal diseases” department, and the Internal Diseases Clinic in “Sveta Marina” University Multiprofile Hospital for Active Treatment JSC – Varna.

16.09.2019

Varna

Respectfully,

Prof. Ivan Donev, Ph.D.

A handwritten signature in blue ink, consisting of several fluid, overlapping strokes that form a stylized, somewhat abstract shape.