

## STATEMENT

In connection with the procedure of holding the academic position of “Associate Professor” in the higher education sphere 7. Health care and sport; professional field 7.1 “Medicine” and “Internal diseases” scientific specialty, for the needs of MU – Varna, “Propedeutics of Internal Diseases” department

A member of the Scientific Jury, the author of the statement – **Prof. Dr. Arman Shnork Postadzhian, Ph.D., Medical University – Sofia, Cardiology clinic, “Sveta Anna” University Multiprofile hospital for active treatment – Sofia.**

**The call for the position “Associate Professor” on the “Internal diseases” scientific specialty** for the needs of of Medical University – Varna, “Propedeutics of Internal Diseases” department, was promulgated in the “State Gazette”, issue 43/31.05.2019.

**The Scientific Jury regarding the call** was appointed with an order of the Rector of Medical University – Varna **No R-109-242/26.07.2019.**

The statement was prepared in conjunction with the Law on the Development of the Academic Staff and the Rules of the conditions and order of acquiring scientific degrees and holding academic positions of MU- Varna.

The only applicant is **Dr. Yavor Kostadinov Kashlov, Ph.D.**, Chief Assistant in the “Propedeutics of Internal Diseases” department, Medical University – Varna.

The submitted set of materials on paper/ electronic media is in conjunction with the procedure of acquiring the academic position “Associate Professor” and the Rules of MU – Varna. I have not detected plagiarism in the scientific materials which have been submitted to me for review. I do not have conflict of interests regarding the present call.

### **Biographical data**

Dr. Yavor Kashlov was born in 1985. His higher medical education he graduated in Medical University “Prof. Dr. Paraskev Stoyanov” – Varna in 2009, Medical faculty. In 2009 he started work as a doctor in *Specialized hospital for active treatment on Cardiology* – Varna. In 2011 he was appointed doctoral student in the “Propedeutics of Internal Diseases” department in MU – Varna. A couple of months later he started working as Adjunct Assistant in the “Propedeutics of Internal Diseases” department. After he won several calls in 2013 he was appointed Regular Assistant. In 2017 he was appointed Chief Assistant on Internal Diseases in the “Propedeutics of Internal Diseases” department.

In January 2017 Dr. Kashlov acquired the scientific specialty “Internal Diseases” (series MUV – 2017 No 3748, reg. No 020604/07.02.2017).

In 2017 he also was awarded **the scientific and educational degree “Doctor” of “Internal diseases” specialty** after defending his thesis on *“Biological markers of necrosis and necroptosis in cardiovascular diseases”*(diploma No 212/ 22.05.2017).

Since 2012 to the present moment Dr. Kashlov has been working in the Internal Diseases Clinic in “Sveta Marina” University Multiprofile hospital for active treatment. From 07.03.2017 after acquiring the Internal Diseases specialty, he started specializing in Cardiology.

### **Scientific research**

In **his scientific research** Dr. Yavor Kashlov **has participated** in two international forums, directly connected with his scientific specialty and its practical application: *The European Congress of Heart Failure, Florence, 2016*, where for the first time at a European congress trends were reported in hospitalization regarding heart failure in Bulgaria in the period 2010 – 2015; and *BIT’s 10<sup>th</sup> Annual International Congress of Cardiology, Rome, 2018*, where for the first time Bulgarian research was reported on necrosis and necroptosis in myocardial infarction. Two new potential biomarkers were presented – HMGB1 and RIPK3.

Dr. Kashlov participates in this call with his scientific production which includes 32 **scientific works**, which are to be reviewed. Their overall impact factor is 26.32. Their distributions is as follows: **publications and reports, published in scientific editions, abstracted and indexed in worldwide data bases with scientific information** – 12 publications, in two of which Dr. Kashlov is a first author; **publications and reports, published in non-abstracted magazines with scientific review or published in edited collective volumes** – 20 publications, in seven of which Dr. Kashlov is a first author, in one he is a second author and in twelve he is a third and consecutive author.

All his publications are in magazines and textbooks, which are in leading areas in the internal medicine field, realized in the period 2014 – 2019. The real publications have been printed in **major medical periodical journals**: “Science Cardiology” – 6, “Heart and lung” – 1; “Scripta Scientifica Medica” – 2; “Bulgarian cancer association journal”- 3; “Studia oncologica” – 2, “Varna medical forum” – 3; “Hematology” – 2; “Journal of IMAB” – 4; “Biosci Trends” – 3; “Metabolic Syndrome and Related Disorders”- 1 etc. He has two published paragraphs, which are in abstracted and indexed journals – “European Journal of Heart Failure” and “European Society of Medical Oncology”, as well as a report in *the International Congress of Cardiology, 2018*.

The total number of **citations** of Dr. Yavor Kashlov’s publications (without self citations) is 26; 25 of them are in international editions and only 1 is in a Bulgarian one; h-index= 2 points. The overall impact factor of the three articles, published in editions with ISI impact factor is 4,934.

### **Main features in Dr. Kashlov’s scientific research**

**Dr. Kashlov’s scientific research** is directed in the following main areas:

- His work is linked with a modern research on a number of biomarkers and their practical application in the Cardiology area – miRNA 208a – a biomarker for the diagnosis of cardiovascular diseases; the serum levels of RIPK3 and troponin I as potential biomarkers for predicting impaired left ventricular function in patients with myocardial infarction with ST-segment elevation and normal troponin I levels prior to percutaneous coronary intervention.

Dr. Kashlov participates in a research, which studies the role of HMGB1 in the pathogenesis of myocardial infarction – STEMI patients have higher levels of HMGB1 compared to healthy individuals. It is demonstrated as well that the higher levels of HMGB1, in admitting STEMI

patients, are connected with an increased risk of death in these patients. HMGB1 has the potential to be a new biomarker to improve the prognosis in STEMI patients.

In another research the possibility NT-pro BNP to be used as a biomarker is explored. It allows evaluation of the gravity of the ischemic heart disease (the changes of NT-proBNP are dynamic in myocardial infarction patients with ST-elevation, treated with primary coronary intervention). As part of the team, Dr. Kashlov also does research on the potential part of *lnc RNA* as biomarkers in myocardial infarction diagnosis. *Long noncoding RNA* has a regulating role on the gene expression of the epigenic control level; transcription and translation of RNA. Some *Long noncoding RNA* has impaired expression in the peripheral blood in patients with acute myocardial infarction and can be useful in diagnosis as well as in improving the prognosis in these patients.

- The scientific interests of Dr. Kashlov extend as well on the role of autophagy on the development of myocardial infarction and heart failure. He does research on the link between autophagy and cardiovascular diseases such as myocardial infarction and heart failure. The mechanisms and the role of this kind of cell death are described in physiological and in pathological conditions. Attention is paid to the therapeutic modulation of autophagy with the purpose of treating myocardial infarction and heart failure.
- Dr. Kashlov demonstrates interest in the diastolic dysfunction and cardiomyopathy in sickle cell anemia. His differentiation of the types of cardiomyopathy in patients with sickle cell anemia is thorough and in detail. Impairment in the diastolic left ventricular function is more common than the systolic dysfunction in patients with sickle cell anemia. This has been deemed an independent risk factor of death in this patient group. Dr. Kashlov also does research in the frequency; the determination of the diagnosis and the treatment of pulmonary hypertension in patients with sickle cell anemia. He acknowledges the importance of pulmonary hypertension in the determination of the prognosis of patients with sickle cell anemia.
- Dr. Kashlov deals with current problems as well, such as: cardiotoxicity – the introduction of effective medicine which is toxic for the heart tissue. He informs us of a new biomarker diagnosis and new therapeutic strategies; reports on the potential role of ferroptosis in the pathogenesis of different cardiovascular diseases. Ferroptosis is a new, relatively unexplored form of cell death with a possible therapeutic and diagnostic potential in many diseases.
- Within the author's interests are also many current issues in **the sphere of Oncology**: the concentration of miRNA in the serum after completing adjuvant chemotherapy has the ability to distinguish early relapse patients from patients without relapse. This is applicable in cancer patients in the II<sup>nd</sup> and III<sup>rd</sup> stage. The reason is in the superiority of these molecules over the standard marker, used up to now – CEA. Dr. Kashlov reports on the potential link between SUV max values and the autophagy marker – Beclin – 1 – in the primary tumour. He demonstrates the prognostic value of SUV max in the liver metastases and regards Beclin – 1 as a potential predictive marker of 5-FU based chemotherapy in patients with metastatic carcinoma of the colon (main pathways and regulators, connected with the cell death and survival, which provide metabolic resistance in the tumours that lead to resistance to chemotherapy and failed treatment of carcinoma).
- Radiotherapy and the types of cell death in the radiotherapy of cancer diseases - The revealing of the exact mechanisms of cell death, induced by ionic treatment will provide opportunities for the development of new target therapies. Their combination with radiotherapy will contribute to the customization and approval of the complex treatment of cancer diseases.
- Autophagy in solid tumours – Although autophagy participates in tumour suppression, it also provides tolerance for cellular stress by allowing the tumour cells to survive in adverse

conditions. Stress-induced autophagy in tumour cells can lead to resistance in treatment and tumour latency with a possible recurrent tumour growth and progression. The clarification of the autophagy role in cancer treatment is crucial, since many anti-cancer treatments are connected with its activation.

- Dr. Kashlov participated in Distress screening of cancer patients. He analyzes the link between the distress levels and the list of problems for cancer patients, as well as the factors which influence the distress levels.

### Teaching activity

The teaching activity of Dr. Kashlov as Chief Assistant in the “Propedeutics of Internal Diseases” department is connected with training medical student in the department and testing and grading their knowledge. His teaching workload for the last five years has been 890 hours student training, which is 180 academic hours per annum. His teaching experience is over 6 years.

### Diagnostic and treatment activity

Dr. Kashlov has over 8 years experience. He has accumulated extensive experience in internal diseases, clinical cardiology and cardiovascular diagnostics. His activity is predominantly connected with internal diseases, where the applicant has shown broad interest. It is obvious from the impressive number of researches and publications that he has an affinity to scientific research. In my opinion especially interesting are those with interdisciplinary focus – clinical and laboratory diagnostics, Oncology, cardiotoxicity of used regimes etc.

### Compliance with the national minimum requirements

Dr. Kashlov has presented a table in conjunction with the Rules of the conditions and order of acquiring scientific degrees and holding academic positions. The fulfillment of the minimum requirements by group of indicators is as follows:

Indicator group	Minimum number of points	Indicator	Applicant
<b>A</b>	50	1. Thesis for the educational and scientific degree “Doctor”.	<b>50</b>
<b>B</b>	100	3. Habilitation thesis - monograph	<b>100</b>
<b>C</b>	200	7. Publications and reports, published in scientific journals, abstracted and indexed in worldwide databases with scientific information.	<b>131.91</b>
		8. Publication and reports, published in non-abstracted journals with scientific review or published in edited collective volumes	<b>100.78</b>
<b>D</b>	50	10. Citations or reviews in scientific journals, abstracted and indexed in worldwide databases with scientific information or in monographs and collective volumes	<b>270</b>
		12. Citations or reviews in non-abstracted journals with scientific review.	<b>40</b>
	40	15. Acquired medical specialty	<b>40</b>

E	30	22. Training of interns, graduate students and doctoral students (seminars and practicums)	30
	<b>200</b>	<b>TOTAL</b>	<b>762.69</b>

**In conclusion** the importance of Dr. Kashlov's results is remarkable, having in mind the large number of publications, focused on unresolved diagnostic and clinical issues in modern internal diseases – biomarkers, Cardio Oncology, cardiotoxicity etc. Having in mind the evidence so far, I hold in high esteem the scientific and applied value of the scientific work of the applicant.

In this call Dr. Kashlov presents as an acclaimed specialist with the established specialty on internal diseases; an educational and scientific degree – Ph.D. – which he has defended successfully. He has climbed the academic ladder from Adjunct Assistant and Chief Assistant and has sufficient initial teaching and clinical experience. The scientific interests of the applicant are extensive and include uniting clinical with instrumental data, which proves the qualities of a scientist with the capacity to master and apply the methods of modern medical practice. His scientific production is quite sufficient by volume, content and significance, novelty and validity of scientific achievements. It meets the requirements of the Rules of the conditions and order of acquiring scientific degrees and holding academic positions and the terms and order of appointing the academic position of “Associate Professor” in Medical University – Varna. The contribution of the scientific production is significant. Proof of that are the positive citations in medical literature.

On these grounds I give my positive vote and suggest to the esteemed members of the Scientific Jury to vote positively for **Dr. Yavor Kostadinov Kashlov, Ph.D., for holding the academic position “Associate Professor”** of the scientific specialty “Internal Diseases” for the needs of Medical University – Varna, “Propedeutics of Internal Diseases” department.



18.09.2019

Prof. Dr. Arman Postadzhian, Ph.D.  
Head of Cardiology Department in the Cardiology Clinic  
in “Sveta Anna” University Multiprofile hospital for  
active treatment – Sofia, Medical University – Sofia

Member of the Scientific Jury