



REVIEW

Regarding

Competition for the academic position "Professor" in the scientific specialty "Medical Biology" for leading courses in Bulgarian and English; field of higher education 4. Natural sciences, mathematics and informatics, professional direction: 4.3. Biological Sciences at the Department of "Medical Biology", MF at MU - Plovdiv - one, announced in State Gazette No. 35 of 19.04.2024.

From

Prof. Dr. Dimitrina Kirilova Dimitrova - Dikanarova, MD, PhD, Professor of Biology at the Department of Biology, MF, MU - Sofia, participating in the composition of the scientific jury, appointed by Order of the Vice Rector of Science and Research of MU-Plovdiv No. R-2300/03.07. 2024 and according to an approved proposal by the FC of the MF, of the MU - Plovdiv (protocol no. 6 of 26.06.2024) holding a competition for the occupation of one academic position "Professor" with one candidate - Associate Professor Maria Hristova Kazakova - Velinova, PhD.

The review has been compiled in accordance with the requirements of the **Law of Academic Development in the Republic of Bulgaria (LADRB)** and the **Approved Guidelines for the Application of the Law of Academic Development in the Republic of Bulgaria (AGALADRB)** - Section "Conditions and procedure for occupying the academic position "Professor", as well as in accordance with the "Regulations for the application of the Law on the academic development in MU - Plovdiv" (2021), containing the required qualitative and quantitative indicators for the occupation of AD "Professor", Rules/example structure of a review for the appointment of AD "Professor" at MU-Plovdiv and Appendix 1 of the Regulations on scientometric indicators for MU-Plovdiv.

For participation in the competition for the occupation of one academic position "Professor" in Medical Biology, for leading courses in Bulgarian and English, published in the State Gazette, no. 35 of 19.04.2024, Associate Professor Maria Hristova Kazakova, PhD, who is also the only candidate who submitted documents, was admitted.

She has submitted all the necessary documents in accordance with the requirements of the Law on the Development of the Academic Staff and the Regulations for the Structure and Activities of the Medical University - Plovdiv. The documents are arranged according to the "Recommended arrangement of scientific works for holding AD "Professor" at MU- Plovdiv".

I. Professional development. Analysis of the candidate's career profile

Maria Hristova Kazakova – Velinova, is a PhD of immunology, specialist in medical biology, associate professor in the Department of "Medical Biology" at the MU - Plovdiv.

Maria Hristova Kazakova completed her higher education at Plovdiv University "P. Hilendarski" with a bachelor's degree in "Molecular Biology" in 2005. In 2006, she obtained the Educational Qualification Master's degree in the specialty "Cell Biology" with excellent result in the training course and from her diploma thesis, and since 2015 she has the Educational Qualification Master's degree in the specialty "Management of Innovations and Research Activity" also with an excellently defended Master's thesis correlating with the problems of medical biology and genetic engineering. After her graduation, during the period: May 2006 - February 2007, Maria Kazakova worked as a biologist, junior expert at PU- "P. Hilendarski". She, after successfully passing a competitive exam, successively held the following academic positions: assistant (November 2007 - May 2014), and chief assistant (from 29.05.2014) in the Department of Medical Biology at the MF, MU - Plovdiv. In January 2013, she acquired a specialty in the field of health care, "Medical Biology", and in October 2013, she also acquired the educational and scientific degree "PhD" in Immunology by defending a dissertation on the topic: "Immunobiological studies on YKL-40 in some inflammatory joint and tumor processes" under the scientific guidance of Prof. Dr. Victoria St. Sarafyan, MD, PhD, DSci. Her postgraduate qualification during the period 2009 - 2024 includes a large number (13) of courses and specializations of varying duration on: principles of flow cytometry, cell culture, PCR and RT-PCR, FACS analysis, medico-biological and social issues related to the diagnosis, treatment and care of people living with HIV/AIDS, personalized medicine, reproductive medicine, etc. She also participated in training courses for project management from the Priority "Health" under European programs. Prof. Kazakova's activity has also been evaluated through prestigious

national awards from various scientific events: for scientific developments; for poster presentations; for a young scientist; and also by winning international scholarships, in connection with her participation in representative scientific forums. Since 2016, after a successful competition, Maria Kazakova has held the post of "Associate Professor" in the Department of Medical Biology, MU-Plovdiv, and since April 2024 she has been elected as the Head of the Department. Associate Professor Kazakova was elected as a member of the Council for Educational Activities of MU-Plovdiv (2018, 2022), and as a Member of the Council for Scientific and Research Activities of MU-Plovdiv (2024).

As of the date of the competition, 2024, Associate Professor Maria Hristova Kazakova, PhD, has 14 years and 6 months of scientific and teaching experience in the field of medical biology, in the specialty of the competition, and has received a very high attestation grade for her overall activity at the MU, Plovdiv (last attestation sheet from 2021), and meets, according to these criteria, the mandatory conditions for occupying AD "Professor" at PU-Plovdiv.

II. General description of the submitted materials for the competition

Associate Professor Maria Kazakova has submitted all the necessary documents and materials according to the "Requirements for occupying the academic position of Professor at MU - Plovdiv" and Appendix 1 to the "Regulations for Academic Development at MU - Plovdiv" (2021). All materials are comprehensive, consistently arranged according to the rules and objectively present the candidate's professional, teaching and research activities.

III. Evaluation of the scientific works of the candidate for the overall academic development

- **Scientific - research activity. General characteristics of scientific production and publication activity**

To participate in the announced competition, Associate Professor Kazakova submitted copies of her scientific works for review; summaries of these works in Bulgarian and English and a **list of their scientific works, of which a total of 58 works are publications in scientific journals, referenced and indexed in world-famous databases with scientific information (*Scopus and Web of Science*), of which 27 publications are articles after AD "Associate Professor" and of**

them: 19 are original articles in refereed and peer-reviewed scientific journals with a high Impact Factor and Q1 or Q2, e.g. *Rheum. Int.*, *Modern Rheumat.*, *Genes*, *Biomedicines*, *Cells*, etc., (of which 5 are included in Habilitation work and 14 are in the group of G indicator), 2 articles are in international databases with Q4 and 6 are articles published in full text in non-refereed journals with scientific review (with required 20 publications, of which 15 are in journals referenced in Scopus and Web of Science, including part 8 with IF, according to the quantitative criteria for AD "Professor", Table.1, outside of these, incl. in Habilitation work). **The total number of points from the published articles of Assoc. Prof. Kazakova in group G is 377** (The total number of points required for Group G indicator, according to Appendix 1, is 250 points).

Assoc. Prof. Kazakova also submits for participation in the competition: 11 peer-reviewed study guides with an international publisher's ISBN number; 1 published university textbook in English; 1 Author's abstract of a PhD thesis for the acquisition of the degree "Doctor"; 1 Habilitation work in the form of scientific publications; 1 chapter of a foreign monograph; publications in electronic format.

IV. Evaluation of monographic work or equivalent publications

Assoc. Prof. Kazakova's scientific works also include a Habilitation thesis - based on scientific publications in refereed and indexed editions in the world **database in Scopus and Web of Sci (5 publications with IF and Q1, Q2, Indicator from Group B, 110 points)**.

In the presented work, the modern concept regarding some mechanisms and components of the innate and acquired immune responses, and in this context the role of representatives of the glycosyl-hydrolase family 18 (GH18) is analysed.

Discussed are: the distribution of members of the Family in different groups of organisms from an evolutionary point of view; their biochemical nature and biological role; the involvement of chitin in the immune response. A special role is assigned to: the extracellular matrix glycoprotein, designated as YKL-40, as a chitinous-like protein, to its synthesis, secretion, concentration in biological fluids, the levels of its spatial organization and the functions of its

chitin-binding region. The role of YKL-40 as a biomarker in inflammatory responses in the course of various diseases (autoimmune, infectious, neurodegenerative, traumatic, neoplastic, etc.) is discussed.

V. Scientific research activity. The main scientific directions

Associate Professor Maria Kazakova's research activities are mainly in the field of cell biology, molecular biology, and immunobiological studies in tumor diseases, inflammatory diseases, and degenerative diseases. Some of the main scientific directions developed by Associate Professor Kazakova and the contributions related to them refer to:

1. Direction: Research and introduction of informative biomarkers and molecular signatures in inflammation and tumorigenesis

In this group of studies, fundamental and clinical studies on extracellular matrix glycoproteins, and mainly on the **glycoprotein YKL-40**, occupy a major place. The importance of **YKL-40** as an important biomarker has been determined and analysed its serum concentration and synovial fluid concentration (in significantly high values) in different groups of patients with inflammatory and degenerative joint diseases. The relationship between: YKL-40, classic clinical-laboratory indicators, pro-inflammatory cytokines (*IL-1 β* , *TNF- α*) in rheumatoid arthritis was confirmed.

In connection with these studies, Assoc. Kazakova and co-authors promise some major contributions regarding:

1. YKL-40 and molecular signatures in oncological diseases and pathological changes in chronic inflammatory processes

A mechanism for the regulation of YKL-40 by miRNA-214 in patients with systemic sclerosis is discussed through *in silico* and *in vitro* experiments in patient blood samples. For the first time, reduced levels of miRNA-214 in plasma correlating with increased levels of YKL-40 in the studied patients are demonstrated, and a model for the transcriptional regulation of YKL-40 in systemic sclerosis is proposed.

When investigating the role of epigenetic mechanisms in pathophysiological processes, a **mechanism for controlling YKL-40 synthesis involving a gene-regulatory axis of sequential interactions between long-chain non-coding RNAs, miRNAs and YKL-40 mRNA in systemic sclerosis has been discussed.**

Through the research of Assoc. Prof. Kazakova and co-authors, for the first time, they investigated the clinical significance of tissue expression of YKL-40 as a prognostic marker in metastatic colorectal carcinoma. The authors found that high serum levels of the protein correlated with a high degree of tumor progression in patients, and increased gene expression was associated with short survival. The obtained results could serve as a marker for patient stratification. Particularly important is the result showing that increased expression of YKL-40 in tumor tissue enhances sensitivity to targeted treatment.

Strong expression of YKL-40 at the tumor front in colorectal carcinoma may serve as a prognostic morphological indicator.

The experimental results of Assoc. Prof. Kazakova and collaborators reveal new information about the role of glycoprotein YKL-40 in metastatic colorectal carcinoma, its potential use as a diagnostic marker with application in predicting the response to therapy and its use as a target molecule for treatment.

2. Studies on lysosome-associated membrane glycoproteins LAMP-1 and LAMP-2 in oncological diseases and pathological changes, in chronic inflammatory process

LAMP-1 and LAMP-2 are supposed to be involved in the processes of autophagy, cell death, neoangiogenesis. Through studies with the participation of Assoc. Prof. Kazakova, it has been proven that high gene and protein expression of LAMP-1 is associated with tumor progression in high-grade gliomas. A more intense cytoplasmic reaction for LAMP-1 was found in histological preparations of glioblastoma multiforme compared to preparations of astrocytomas, indicating that the expression of the protein is related to the degree of tumor development. LAMP-1 has been suggested to play a role in tumor progression.

It is suggested that studies on the concentration of LAMPs glycoproteins and YKL-40 in serum and cerebrospinal fluid, and the mRNA levels of YKL-40 in leukocytes of patients would be relevant in acute infections of the central nervous system. These facts determine new future directions in the work of the scientific team.

2. Direction: Cell biology and cell metabolism

1. Cell biology

Assoc. Prof. Kazakova and co-authors determine: the biological action of some new aldose reductase inhibitors (fluorenyl spirohydantoins), the structure and biological properties (cytotoxic effect on human tumor cell lines) of substituted fluorenyl spirohydantoins.

2. Cellular metabolism

The role of mitochondria and a number of exogenous and endogenous factors (proinflammatory cytokines as a result of an activated immune system, oxidative stress, etc.) that can damage or weaken their function has been investigated. Assoc. prof. Kazakova participates in the new direction developed by the colleagues of the Department of Medical Biology, related to the study of bioenergetic and metabolic pathways in the cell (by measuring mitochondrial activity in living cells). Thanks to these studies, the following contributions have been made:

For the first time, the authors report a metabolic profile in patients with autism spectrum disorder, changes in mitochondrial activity in a Bulgarian cohort and correlation with YKL-40 levels.

Assoc. Prof. Kazakova and co-authors found that mitochondrial activity in patients with Parkinson's disease improves after treatment and an interaction with YKL-40 is assumed. Quantitative expression and protein analysis of markers of neuroinflammation (YKL-40) and autophagy (LAMP-1 and LAMP-2) and evaluation of differences in their levels between two groups of patients treated by different therapeutic regimens were performed. The authors

suggest that YKL-40 gene and protein levels in combination with changes in mitochondrial function could serve as an additional factor in monitoring the clinical course of the disease.

New data are also presented regarding the presence of mitochondrial dysfunction in isolated PBMCs from newly diagnosed rheumatoid arthritis patients.

It was found that increased ATP values in the group of patients treated with JAK-inhibitors correlated with improvement in clinical and laboratory tests. The authors suggest that the amount of ATP produced can serve as an indicator for monitoring the course of the disease, defining new perspectives for monitoring and therapy in such patients.

- ***Scientific activity. Dissemination and application of the candidate's scientific and practical achievements among the scientific community***

Assoc. Prof. Kazakova has reported the results of her research work at national and international scientific forums. She participated in 98 scientific congresses and conferences (33 international).

- ***Reflection (citation) of the candidate's publications in the national and foreign literature:***

16 of Assoc. Prof. Kazakova's articles, with which she participated in the competition for AD "Professor" have been cited (after 2016) 124 times, and 7 reviews of articles have been presented, which corresponds to 262 points in group D (Citations or reviews in scientific publications, referenced and indexed in world-famous databases with scientific information (Scopus and Web of Science) or in monographs and collective volumes, if 100 points are required according to the quantitative criteria for AD "Professor", Table 1.). The fact that 5 of the publications (in the journals "*Int.J.Mol.Sci*", "*Genes*", "*AP IS*", "*Rev.NeuroSci*" and "*Folia Med*") are cited by 10 and more than 10 foreign authors is highly positive for the importance of the published articles. Prof. Kazakova also presents a report based on Scopus data, showing a total number of citations of 221, as well as H-index=11.

Assoc. prof. Maria Kazakova participated in: 4 national scientific and educational projects, 2 international scientific projects, and was the Project Manager, Supervisor of 2 national scientific projects and 2 international scientific and educational projects, with attracted funds for the supervised projects. These data prove both her capabilities for teamwork, methodical and organizational leadership, and financial support of the experiments.

Assoc. Prof. Kazakova has acquired the specialty "Medical Biology". The list of scientific works of Associate Professor Kazakova includes 11 teaching manuals in medical biology and parasitology as co-author (after associate professor). All the mentioned study guides and one parasitology textbook in English are currently used in teaching at MU-Plovdiv.

Assoc. Prof. Maria Kazakova is also the co-author of 3 study guides in biology for candidate-students.

Assoc. Prof. Kazakova is also the scientific supervisor of distinguished students (2), scientific consultant of a graduate student (1), scientific consultant in the preparation and defense of scientific reviews by students (4), scientific supervisor of two PhD students (1 defended and 1 with a procedure in course), supervisor of Medical Biology specialization students (1 acquired specialization and 1 in the course of specialization).

The total number of points in indicator group E of the candidate is 394.29 points.

VI. Educational - teaching activity

Assoc. Prof. Maria Kazakova has the necessary medical and biological competence, language culture and skills for conducting educational work. She participates in the training in the discipline "Medical Biology", for students of medicine, dental medicine and pharmacy from the first year of the MU - Plovdiv, in Bulgarian and English. She develops in English a part of a lecture course on medical biology, prepares teaching aids, illustrates and conducts practical exercises in biology and parasitology for medical students for the English language education. Assoc. Prof. Kazakova is an examiner (13 years) of candidate - student competitive works in

biology; she is the chairman of the Commission on Biology for candidate students in Bulgarian (2 years) and the Commission on Biology for English language studies (1 year). She is responsible for the scientific activity of the Department of Medical Biology. She is a member of the Council for Educational and Research Activities of MU-Plovdiv.

Her study load in the last two academic years, according to the presented report, corresponds to 786 points. Academic position held: Associate Professor since 2016 – 7 years (700 points).

Total number of points in INDICATORS GROUP: 1486.

Total number of points from all indicators: 2679.29.

VII. Critical notes and recommendations

I have no critical remarks about the candidate. I recommend that she pass on the important medico-biological knowledge she has, as well as the accumulated valuable experience, to her colleagues, to her students, and to the PhD students, preserving the spirit of collegiality and high professionalism established in the Department of Medical Biology, MU-Plovdiv.

Conclusion:

Associate Professor Maria Hristova Kazakova-Velinova, PhD, who is also the only candidate in the Competition, was admitted to participate in the competition for the occupation of one academic position "Professor" in Medical Biology, for the teaching of Bulgarian and English.

Associate Professor Kazakova has the necessary scientific and teaching experience in the field of medical biology, in the specialty of the competition, and has received a very high attestation grade for her overall activity at the MU - Plovdiv, meeting all the criteria of the mandatory conditions for occupying the Academic Position "Professor" at MU-Plovdiv. She obtained the specialty "Medical Biology" in the field of health care, as well as the educational and scientific degree "PhD" in Immunology. She has consistently occupied the academic positions: assistant, chief assistant and associate professor at the Department of Medical Biology of the MU - Plovdiv. Associate Professor Maria Kazakova's research activities are mainly in the field of cell biology, molecular biology and immunobiological studies in tumor diseases, inflammatory joint

diseases and those of the CNS, and degenerative diseases. Assoc. Prof. Kazakova is a trained professor in the Department of Medical Biology of the Medical Faculty, MU of Plovdiv and possesses the necessary competence, professional and organizational qualities, language culture, and skills for conducting educational work with students in Bulgarian and English.

She has its own appearance in its teaching and research activity, which is included in the multifaceted activity of the Department of Medical Biology.

The analysis of the above data shows that: the scientific production and publication activity of Assoc. Prof. Maria Hristova Kazakova, as well as the other scientometric criteria in their entirety, collect and exceed the required total number of points according to the mandatory requirements.

The review of the materials presented by Associate Professor Kazakova regarding her participation in the competition for the academic position "Professor" in Medical Biology for the needs of teaching Bulgarian and English at the Department of "Medical Biology", MF at the MU - Plovdiv allows me to state that the overall activity of Assoc. Prof. Maria Hristova Kazakova, PhD, meets the requirements of **Law of Academic Development in the Republic of Bulgaria (LADRB)** and the mandatory and specific conditions and scientometric criteria for the academic position "Professor" in the "Regulations for the Organization and Activities of the MU - Plovdiv", **and fully convinced to support before the members of the Honourable Jury the candidacy of Assoc. Prof. Maria Hristova Kazakova, PhD, for awarding her the academic position of "Professor".**

Sofia

Signature: 

Заличено на основание
Чл.5 §1, б."В" Регламент (ЕС)2016/679

01.09. 2024

(Prof. Dr. D. Dimitrova-Dikanarova, MD, PhD)

Приложение 1. Table1 относно ЗАДЪЛЖИТЕЛНИТЕ МИНИМАЛНИ НАУКОМЕТРИЧНИ ПОКАЗАТЕЛИ, както и тези на участващата в Конкурса за АД Професор в МУ-ПЛОВДИВ - доц.Казакова, ЗА ОБЛАСТ НА ВИСШЕТО ОБРАЗОВАНИЕ

4. ПРИРОДНИ НАУКИ, МАТЕМАТИКА И ИНФОРМАТИКА Научна специалност "Медицинска биология" (след рецензията)

ГРУПА	ПОКАЗАТЕЛИ	СТОЙНОСТ	Професор	ТОЧКИ НА КАНДИДАТА Доц. Мария Казакова
А	1. Дисертационен труд за присъждане на образователна и научна степен "доктор"	50	50	50
Б	2. Дисертационен труд за присъждане на научна степен "доктор на науките"	100		
В	3. Хабилитационен труд - монография	100	100	110
	4. Хабилитационен труд - научни публикации в издания, които са реферирани и индексирани в световноизвестни бази данни с научна информация (25 т. - Q1, 20 т. - Q2, 15 т.- Q3, 12 т. - Q4, 10 т. за публикация в списание с SJR БЕЗ IF)			

Г	5. Публикувана монография, която не е представена като основен хабилитационен труд	30		
	6. Публикувана книга на базата на защитен дисертационен труд за присъждане на образователна и научна степен "доктор" или за присъждане на научна степен "доктор на науките"	20		
	7. Публикации и доклади, публикувани в научни издания, реферирани и индексирани в световноизвестни бази данни с научна информация (25 т. - Q1, 20 т. - Q2, 15 т. - Q3, 12 т. - Q4, 10 т. за публикация в списание с SJR БЕЗ IF)		250 точки 20 статии В списания реферирани в Scopus и/или Web of Science, в т.ч. 8 статии с IF	377
	8. Публикувана глава от книга или колективна монография	15		
	9. Изобретение, патент или полезен	25		

	модел, за който в издаден защитен документ по надлежния ред			
	10. Публикувана заявка за патент или полезен модел	15		-
	Общо за Г			377
Д	11. Цитирания или рецензии в научни издания, реферирани и индексирани в световноизвестни бази данни с научна информация или в монографии и колективни томове (Scopus и Web of Science)	2	100 точки	262
Е	12. Придобита научна степен "доктор на науките"	75		
	13. Ръководство на успешно защитил докторант (п е броят съръководители на съответния докторант)	50/п		50
	14. Участие в национален научен или образователен проект	10	150 точки	50 + - придобита специалност

	15. Участие в международен научен или образователен проект	20	-2 защитили докторанти - 1 научен проект - 1 учебник/посobie	40 1 учебник + 11 учебни пособия
	16. Ръководство на национален научен или образователен проект	20		40
	17. Ръководство на международен научен или образователен проект	50		100
	18. Привлечени средства по проекти , ръководени от кандидата	1 т. за всеки 5000 лв.		331 110лв.= 66,2
	19. Публикуван университетски учебник или учебник, който се използва в училищната мрежа	40/п		6,66
	20. Публикувано университетско учебно пособие или учебно пособие, което се използва в училищната мрежа	20/п		41,43
	Общо за Е			394,29
	Преподавателска дейност:			

Ж	Учебна натовареност (лекции и упражнения):		360 точки (за последните 2 г. X 1т/час)	786
	Академична длъжност:		200 точки (Доцент – 100 т. за 1 год.)	700
	Общо за група Ж			1486
	ОБЩО:		1210	2679,29

Заличено на основание
Чл.5 §1, 6."В" Регламент (ЕС)2016/679