

# REVIEW

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**To the candidate:** Assoc. Prof. Dr. Milka Mileva, Ph.D., competition for filling the academic position of "Professor"

Prepared on the basis of Order No. 52/28.04.2023 of The Stephan Angeloff Institute of Microbiology (IMicB), Bulgarian Academy of Sciences, for Scientific Jury and Decision of the Scientific Jury for determining and selecting reviewers and for opinions.

## **1. Procedural rules.**

All documents are submitted in accordance with the Regulations for the Application of the RSARB of the Republic of Bulgaria and the BAS, as well as in accordance with the Additional Requirements of the IMicB to the BAS. They are prepared according to criteria, the data are precisely calculated according to the required criteria in points from the candidate, they are presented in text, and in tables, they are clearly and accurately arranged. The competition for the academic position "Professor" is in the field of higher education 7. Health care and sports, professional direction 7.3. Pharmacy from the Law on the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB) for the needs of the Department "Virusology", Laboratory "Biological response modifiers and pathogenesis of viral infections", promulgated in "Government Gazette", (Government Gazette, issue 21 of 03/07/2023), IMicB - BAS. The Scientific Council of The Stephan Angeloff Institute of Microbiology has selected a Jury for this competition and with Protocol No. 45 of 04/27/2023 offers it to the Management of The Institute, respectively, for issuing the above-mentioned Order. The whole procedure was carried out correctly and according to the legal requirements.

## **2. Biographical data for Associate Professor Milka Mileva, PhD**

Associate Professor Milka Mileva was born in the city of Karnobat, graduated from the University of Plovdiv with a degree in Chemistry (1993), successively worked at the Bulgarian Academy of Sciences, MU-Sofia (developing a doctoral dissertation at the Department of Physics and Biophysics of the Faculty of Medicine, MU-Sofia). In 2002, she successfully defended her doctoral dissertation, and through a competition she was appointed

to the "Stephan Angeloff" Institute of Microbiology - BAS, Section "Microbial Biochemistry", as a Chief Assistant, and in 2011 she won a competition for AD "Associate professor" in the Department of "Virology ". He is currently the Head of the Laboratory "Biological Response Modifiers and Pathogenesis of Viral Infections" (since 2017). Associate Professor Mileva is a well-known scientist at home and abroad, a teacher of students for master's and educational programs at SU, MU-Sofia, Southwest University and at the Medical College "Yordanka Filaretova" at MU. She is the Chairperson of the General Assembly of Scientists at IMicB (Institut in microbiology - BAS) from 2017 - until now; He is a member of the Supervisory Board of The Stephan Angeloff Institute of Microbiology - 2020 - until now; He is active as a member of nine scientific juries for the academic position "Professor", "Associate Professor ", and "Doctor"; Member of 10 Examination Committees for the selection of assistants and conducting doctoral examinations, etc. He is the supervisor of 2 doctoral students who have successfully defended their dissertations, 1 dismissed with the right to defend and 1 with an ongoing procedure. She has a significant scientific activity through her participation with reports and posters at more than 120 conferences at home and abroad, 76 of which are after her appointment as associate professor (or for the last 11 years). She was an expert in 35 committees. He is fluent in several foreign languages.

### **3. General description of the presented materials: monographs, articles, certificates and patents, textbooks, etc., classified by subjects**

Associate Professor Milka Mileva submitted the following number of materials with documents for review in the competition, as follows:

- Total number of publications 128 publications, of which 49 with IF
- Published sections/chapters of books or collective - 6;
- Issued textbooks and study aids – 4;
- Dissertation work for the award of "Doctor" - 50 points;
- Total number of citations = 716;
- Participation in scientific forums - 156 conferences, symposia, congresses, 110 posters and 46 oral presentations;
- IF of publications – total = 80,851
- H index = 13 (Scopus), In her reference she gives a factor =15, formed by citations in other databases as well.

### **Reviewer Analysis:**

A significant number of scholarly publications are submitted that exceed the requirements for a professorship. Analysis by criteria shows the following results:

**A) Scientific-metric indicators are according to evaluation criteria and point evaluation of the published materials:**

- articles replacing habilitation thesis are 13 articles, in 10 of them the candidate is the first or corresponding author (111.78 points-criteria V);
- articles with original scientific contributions in refereed scientific journals = 7, of which in 6 she is the first or corresponding author, respectively = 112.09 points according to G criteria;
- articles in non-refereed journals with scientific review - 19 articles, in 11 first or corresponding authors - 137.44 points; Criteria G8
- Criterion G 9 - 2 chapters of collective monographs, in 11 first or corresponding author, 13.33 points.

**B) Analysis of citations (I indicate those by criteria and point evaluation):**

Total number of citations = 716; Of them by criteria and formed points

- Criterion D10 - Citations in scientific publications, referenced and indexed in 50 global databases, form 750 points;
- Criterion D11 Citations in monographs and collective volumes with scientific review - 13, form 130 points;
- Criterion D12 Citations in non-refereed journals with scientific review - 16, form 80 points;

**C) Analysis according to criteria E and calculation of points as follows:**

Criterion E14 - Guidance of a successfully defended doctoral student - 2 PhD student - 40 points

Criterion E16 - Participation in a national scientific project - 105 points

Criterion E 18 - Management of a national project - 120 points

Criterion E 19 - Management of an international project - 40 points

Criterion E 20 - Published university textbook - 8 points

**Total number of points for participation in the competition for the academic position "professor" 1567.64 points (out of required 750)**

**D) Evaluation of section 3:** a) I accept the distribution of the materials for the competition of candidate associate professor Milka Mileva. The materials are presented in lists according to the relevant criteria mentioned above. They are correctly presented in tables according to the requirements of the Regulations of the Institute of Microbiology, BAS. The total number of

points (= 1576.64) exceeds that of the requirements for a professor (750); c) The total number of publications meets the requirements for a professorship; After habilitation as an associate professor, 42 publications were presented, which I review below, of which 10 were the first author; d) The attached 13 publications replacing habilitation work meet the requirements for a professorship. On some of the publications, associate professor Mileva is the first author, which determines her independent and significant role in their research and publication and determines my positive assessment; e) Citations are clearly indicated, they are accurately and correctly presented by sections and show a significant number of them in international and refereed scientific journals. Citations exceed the requirements for professorship. f) The scientific activity of associate professor Mileva through the development of sections of monographs and textbooks is positive; g) Associate professor Mileva is the supervisor of 2 defended dissertations, which meets the requirements for a professorship; in addition, she supervises 1 more PhD student dismissed with the right of defense, 1 in an ongoing procedure, which determines the active work of associate professor Mileva in training young personnel in science and education. h) I also positively evaluate the scientific activity of associate professor Mileva in the direction of development of our and international scientific projects; She presents in a table that she is the Head of 5 national and 1 international scientific projects; and by this indicator, she exceeds the additional criteria for the academic position of professor for the growth of the academic staff of IMicB. i) I assume a Harish index = 13, which is related to the long-term scientific work of the candidate, publication in World Scientific Journals and citations by leading scientists of her publications. k) The impact factor of the publications is = 80.85 (total), I accept it and according to my calculations it corresponds to the scientific articles presented in the documents.

#### **4. Publications and other equivalent achievements outside the previous procedures for academic positions and scientific degrees. Posts after the last procedure.**

The presented documents reflect significant scientific and educational activity of the candidate after her election as an associate professor in 2011. I have mentioned them above, but here I will repeat the following facts: 42 publications, in 30 she is a leading or corresponding author; 2 dissertation students who defended their doctoral theses, 1 dismissed with the right to defend and 1 in current doctoral studies; 5 National and 1 international scientific projects, 1 textbook;

## **5. General characteristics of the candidate's scientific, teaching, and scientific-applied activities.**

Analysis of the publications after the election as associate professor - total number 42. The leading directions of scientific research are four and a significant number of the publications focus on different mechanisms of action of pharmacological agents. The attached 13 articles replacing habilitation work were published for the period of 2019-2020, most in 2021 and 2022, which determines the contemporaneity of her studies. They are in the directions below. In 10 of them, she is first or corresponding author. Assoc. prof. Mileva applies tables detailed with calculations of points for each article and IF, divided by authors, which is correct and accurate according to the requirements for this competition (analysis of 42 publications, not reviewed in previous competitions).

**5.1. Oxidative stress and oxidative mechanisms** of liver and lung damage, blood plasma and stomach during experimental influenza infection and their influence by xenobiotics (specific inhibitors of influenza viruses rimantadine, Tamiflu - individually and in combination with vitamin E, vitamin C, polyphenols, precursors of glutathione); A group of publications presents the results of research on redox processes as a key mechanism in maintaining cellular homeostasis and the normal functioning of the body. The authors found that disturbances in this mechanism have a decisive role in the pathogenesis of malignant, neurodegenerative, atherogenic, autoimmune diseases, diabetes, etc. (Publications Nos. 3, 4, 8, 9, 12, 16, 17, 21). Related to these are the original studies on the role of glutathione in oxidative stress mechanisms (publications №. 32, 39). Research on the cytotoxic, genotoxic and antioxidant effects of various substances isolated from plants such as *Ginkgo biloba*, rose, etc., is modern, up-to-date and with contributions. (Publications № 1, 2, 5, 6, 11, 14, 15, 22, 35). Antioxidant mechanisms of action of various natural products have been studied and published (publ. № 25, 27, 28, 29, 37, 40, 41). With significant contributions in the field of viral infections are the works of associate professor Mileva and studies of new mechanisms of action of both antiviral drugs established in the clinic (rimantadine, Tamiflu) and natural products (pub. no. 4, 7, 10, 23, 24, 34, 36, 38, 39). To them I add the progress of the candidate in microbiology by researching new markers for infections with influenza viruses (No. 34). A current research direction is the investigation of endogenous cannabinoids in modulating stress responses (pub. no. 13). After inoculation of male white mice with 10 MLD50 (mouse lethal doses 50) of an adapted laboratory strain of influenza virus A/Aichi/2/68 (H3N2), influenza infection was found to increase oxidative stress markers in white and liver, as well as in the stomach of infected animals, reduces the level of glutathione

and alpha tocopherol, as well as the activity of the antioxidant enzymes catalase and superoxide dismutase. These changes are supported by the histological picture of disturbed cytoarchitectonics in liver and lung, kidney, stomach, and testis (publ. № 3, 4) Ethyl acetate (EtOAc), n-butanol (n-BuOH) extracts of roots and aerial parts of the plant *Geum urbanum* L. were tested on Burkitt's lymphoma cells (BLC) to verify their effects on oxidative stress and cell survival in an oxidative stress experiment. For the first time, the results provide new evidence for a direction in the therapy of lymphomas.

**5.2.** Role of H2 blockers in conditions of copper deficiency in experimental model of ulcerogenesis (general list publication reviewed before this competition).

**5.3.** Potential anti-cataractogenic agents – vit. E, captopril, He-Ne laser irradiation in the setting of diquat-induced cataractogenesis in rabbits (21).

**5.4.** Biological activities of essential oils and plant extracts (included in the analysis of 5.1). They demonstrate new oxidative activities and contribute to the expansion of knowledge about new biologically active substances.

The analysis of the scientific publications published after the habilitation for associate professor shows that their results are up to date, dedicated to new mechanisms of various substances with utility for experimental and clinical sciences. Original facts have been published about viral infections and drugs/biologically active substances for the treatment of various diseases such as herpes, influenza incl. malignant. I positively evaluate the articles presented for review, I highly value the state-of-the-art methods, as well as the implementation of new approaches and ideas in the developments. The high impact factor of the published works, in combination with the large number of citations, including international ones, outlines their national and international significance for science.

**6. Teaching work of Assoc. prof. Milka Mileva.** She has been teaching students for decades at several universities, incl. in SU and MU-Sofia, as her teaching activity is continuous. She has sections written in a textbook. There are two doctoral students who have defended their PhD theses and 1 graduate with the right to defend. I give a positive assessment of her teaching activity.

## **7. Characterization of the main achievements of the candidate**

\* In the field of oxidative stress –mechanisms, new approaches, new methods. It is important for medical, biological, genetic sciences.

\* In the field of Pharmacology – new mechanisms of drugs for the treatment of viral disease, ulcer, cataracta, tumor diseases, etc.

\* The large progress was made by Dr Mileva in the field of discovery of new mechanisms of various substances from plants with their applications in medicine.

\* Taken together, the studies of Dr Mileva are very important for the further progress of medico-biological science, as well as for the clinic of viral and oncological diseases.

**7.1.** Reverberation of the candidate's results in the works of other authors. Numerical indicators - citations (without self-citations), impact factor, SJR, etc. similar. I have presented the numerical data above. The analysis shows that the presented citations are correctly given, distributed in tables, without self-citations and reflect the importance of assoc. prof. Mileva scientific research for experimental and clinical sciences. The overall impact factor is high, the Harish index is high. My assessment for this section of the review is positive.

**7.2.** In the case of collective publications, assess the candidate's contribution. Associate professor Mileva has presented in tables the distribution between the authors of the collective publications, she has calculated both her points and IF on this basis. In these tables, the articles are arranged according to the journal requirements, which is correctly and precisely done by the candidate.

## **8. Reviewer's critical notes and recommendations.**

8.1. The document of author analysis of publications is large and it is not clear in some parts.

8.2. There are not data in documents about the specializations abroad of the candidate.

8.3. I recommend of Dr Mileva to publish in one monography her large experience in the field of oxidative stress, viral diseases and effects of drugs. In addition, my recommendation is going to her experience as a teacher, she to organize at least one course on oxidative stress for students.

## **9. Personal impressions of the reviewer about the candidate.**

I have known Associate Professor M. Mileva since more than 20 years ago, when she worked as an assistant and defended her doctoral dissertation at the Faculty of Medicine - Sofia. She is an erudite, accurate, hardworking, and self-critical scholar. She developed new methods for the first time in the Department of Physics and Biophysics, put a lot of effort and time into innovations in science. Later, when she moved to work at the BAS, she showed the same qualities and activity at various national and international congresses. I have been working for decades in the field of much of her research, those with a pharmacological focus, glutathione and oxidative stress, incl. viral infections and I have admired her experience and determination to do science, to constantly generate new ideas and conduct cutting-edge research, to educate young people. My personal impressions are excellent.

## **10. Conclusion.**

The candidate meets the set of criteria and indicators for the occupation of the academic position of "PROFESSOR" according to the ZRASRB and the Regulations for the implementation of the ZRASRB of the Ministry of Education, BAS and IMicB. Associate Professor Milka Mileva has had continuous scientific and teaching work for 30 years, with significant achievements in experimental and clinical sciences, with indicators of scientific publications, doctoral students, scientific projects, and reports at congresses exceeding the requirements for a professor. Associate Professor Mileva is a scientist with national and international authority, with proven activity in various expert councils, juries for habilitation, and doctoral studies, with successfully implemented new methods and approaches for the purposes of the scientific achievements reviewed above. She is a respected teacher by students and colleagues.

**I convincingly recommend to the scientific jury to elect associate professor Dr. Milka Mileva as a professor in the field of higher education 7. Health care and sports, professional direction 7.3. Pharmacy from ZRASRB for the needs of the Department of "Virology", Laboratory "Biological response modifiers and pathogenesis of viral infections" at The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences.**

**Date: 25/05/2023**

**Sofia**

**Reviewer:**

**Prof. Nadka Ivanova Boyadjieva, MD, PhD, DSci**