

STATEMENT

Concerning: the scientific contributions, the teaching, and organizational activities of Assist. Prof. Maya Margaritova Zaharieva, Ph.D., at the Department Infectious Microbiology, Laboratory Cytotoxicity and Signal Transduction, the Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences – candidate in a competition for the academic position "Associate Professor" in a professional field 4.3. Biological Sciences (Microbiology), published in the Official State Journal, no. 47 of 22.05.2020.

One candidate participates in the announced competition for Associate Professor in the above field – Assist. Prof. Maya Margaritova Zaharieva, Ph.D. The documents of the candidate are regular, and the selection procedure started with a meeting of the Scientific Jury on 24.07.2020.

Prepared by: Assoc. Prof. Vesselin Kussovski, PhD, specialist microbiologist at the Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences.

I declare that there are no conflict of interest between me and the candidate.

In 2001 Maya Zaharieva graduated Faculty of Pharmacy, MU-Sofia, Bulgaria as a Master Pharmacist. In 2008 she received the Educational and Scientific Degree "DOCTOR" in the scientific specialty: "Pharmacology". Two scholarships are important for her scientific growth: Erasmus/Socrates Scholarship for Graduate Students 2001 and DAAD Scholarship for Doctoral Students 2004-2005 at the German Cancer Research Centre, Heidelberg, Germany. Both specializations in 2012 and 2015 at the Institute for Agricultural and Fisheries Research in Merelbeke, Belgium are extremely useful.

For participation in the competition, Assist. Prof. Maya Zaharieva, PhD presents a detailed report on her overall activities, specifically for participation in the competition are included 28 scientific papers (21 articles with JCR-IF; 1 publication in journal with SJR, 3 chapters from books; 3 articles in proceedings of international forums). The total IF of her scientific publications is 45.724, and the H-factor - 9. The candidate is the first author in 8 publications, of which: 5 articles with JCR-IF; 1 publication in SJR journal, 1 book chapter; 1 article in proceedings of congresses. The positive response among the world scientific community is expressed in 235 citations as of 17.07.2020. The scientific production of Assist. Prof. Maya Zaharieva, PhD covers all the minimum requirements in the Academic Staff Development Law in Republic of Bulgaria, and the additional criteria for the growth of the academic staff in IMicB-BAS, as some of them are exceeded many times.

The participation of Dr. Maya Zaharieva in national and international scientific forums (36 in total), where she participated as a co-author of 22 reports and 34 posters is very active. In 19, out of all 56 scientific presentations, she is the first author.

Her research and scientific potential, Dr. Maya Zaharieva develops in a number of successfully implemented and completed research projects. She is the research supervisor of three of the 14 projects in which she participates. Of particular importance is the project led by her and successfully implemented for the creation and

development of a Laboratory "In vitro cytotoxicity and signal transduction" under the Equipment Subsidies Program of the Alexander von Humboldt Foundation, 10.2014-10.2019. It should be noted her active and creative participation in projects at the Bulgarian National Science Fund, research funding programs at the Medical University of Sofia and Sofia University "St. Kliment Ohridski", Center for Competence "Clean & Circle", the National Research Program "BioActiveMed" and youth support programs scientists at BAS.

The main scientific contributions from the activity of Assist. Prof. Maya Zaharieva, PhD are related to research in the field of experimental chemotherapy of malignant diseases and concomitant bacterial infections. The studies are focused on the selective antineoplastic and antibacterial activity of synthetic compounds from the group of alkylphosphocholines and a series of plant extracts and biologically active substances (BAS) isolated from various plants with potential application in human medicine. It is important to clarify the key role of the Rb signaling pathway for the antineoplastic effect of the alkylphosphocholine erufosine and the ability to predict this effect on the base of the phosphorylation status of the Rb protein. The potential of eleven triterpene saponins, which accumulate in the roots of *Gypsophila trichotoma* L., to potentiate in non-toxic concentrations the antineoplastic effect of the clinically administered cytostatic etoposide in Hodgkin's lymphoma cells, which represents a new contribution to the pharmacological characteristics of these BAS.

In the field of antimicrobial activity, antibacterial activity of the alkylphosphocholine erufosine against metacillin-resistant (MRSA) and susceptible strains of *Staphylococcus aureus* (MSSA), as well as its ability to inhibit the formation of a biofilm of MRSA, was demonstrated for the first time. The results obtained are important in view of the development of erufosine as a chemotherapeutic for the treatment of cutaneous T-cell lymphoma, the pathogenesis of which is accelerated in infection of patients with pathogenic strains of *S. aureus*. The ethyl acetate extract of the plant *Graptopetalum paraguayense* shows strong activity against *S. aureus*, which is a prerequisite for obtaining of natural products from this plant for medicinal purposes. In a series of scientific studies, the antibacterial activity of the newly isolated from *Geigeria alata* compound 3,4,5-tricafeoylquinic acid against penicillin-sensitive, penicillin-resistant *S. aureus* and MRSA strains was established for the first time. Moreover the antibacterial potential of extracts of newly isolated strains of microalgae of the species *Poterochromonas malhamensis*, *Chlorella* sp., *Micractinium* sp., *Tetradismus* sp. and *Desmodesmus* sp. against pathogens of the species *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *S. aureus* and *Streptococcus pyogenes* was proved too. The antibacterial activity of human neutrophil peptide alpha-defensin 2 in pharmacopoeial buffers with different pH against pathogenic *E.coli* has been studied and described for the first time, which is an important contribution to the development of a suitable pharmaceutical form.

In the field of toxicological analyzes, it is essential that ethyl acetate extract from the plant *Geum urbanum L.* does not show toxic effects on intestinal epithelium and Peyer's patches. Cytotoxicity of saponins isolated from the roots of the plant *Gypsophila trichotoma L.* on the standardized cell line of normal murine fibroblasts CCL-1 is not found. It is demonstrated the lack of cytotoxic effect on the cell line CCL-1 of the coating of ophthalmic prostheses with Al₂O₃ nanolayer showing antibacterial and antifungal activities.

The contribution of the candidate in modeling the proliferation of malignant cells and metabolic activity in bacteria with mathematical software MAPLE is significant. For the first time in Bulgaria, software has been created that overcomes the shortcomings of the linearization of nonlinear kinetic models. The results are published in an international journal with impact factor and have a fundamental and applied importance. The created programs open new horizons for the use of mathematical modeling methods for scientific and applied purposes in the field of oncopharmacology, toxicology and infectious microbiology.

The prospects presented by the candidate for future research are impressive. Her work will continue in the following areas: characterization of the toxicological profile of natural and synthetic substances with proven antimicrobial activity in the implementation of three ongoing projects; study of the antineoplastic and antimicrobial activities and elucidation of the mechanism of action of new drug candidates of natural and synthetic origin within four ongoing projects; in vitro study of interactions between bacterial pathogens/toxins and host cells associated with the carcinogenesis of certain neoplasms: one project.

CONCLUSION

Based on my acquaintance with the attached official documents and the presented scientific activities, their significance for science and practice, the scientific and applied contributions and methodological approaches, etc., I find that the scientific production of Dr. Maya Zaharieva exceeds the requirements of the Law for the Academic Staff Development Law in Republic of Bulgaria, the Regulations for its implementation and the regulations of BAS and IMicB-BAS. I believe that the candidate is a well-established and very successful scientist and expert in these areas of biomedicine.

Based on the above arguments, I strongly recommend Assist. Prof. Maya Zaharieva, PhD to take the academic position of "Associate Professor" in a professional field 4.3. Biological sciences (Microbiology).

Sofia
21.08.2020

Prepared by:
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