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To

The Chairperson of Scientific Jury determined by order N_2 I – 39/23.04.2021 of the Director of Institute of Microbiology "Stefan Angelov" - BAS

REVIEW

By: Prof. Radostina Ivaylova Alexandrova, MSc, PhD, Leader of a work group in Pathology Department, Institute of Experimental Morphology, Pathology and Anthropology with Museum — Bulgarian Academy of Sciences, Part time lecturer in Sofia University "St. Kliment Ohridski", Faculty of Biology; Lecturer in PhD School of Bulgarian Academy of Sciences; Member of the Scientific Jury determined by order № I — 39/23.04.2021 by the Director of the Institute of Microbiology "Stefan Angelov" — Bulgarian Academy of Sciences (IMICB-BAS).

Regarding: competition for the for the occupation of the Academic position "Associate Professor" in the Department of Immunology, Institute of Microbiology "Stefan Angelov" - BAS, in the field of "Natural Sciences, Mathematics and Informatics", Professional field 4.3 "Biological sciences", specialty "Microbiology".

General presentation of the documents in the contest

In the competition announced in the State Gazette No. 20 of 09.03.2021 for the academic position of "Associate Professor" for the needs of the Department of Immunology at IMICB-BAS, only one candidate submitted documents — Assistant Professor Nikolina Mihaylova Mihaylova, MSc, PhD, from the same Department. The set of all necessary documents precisely prepared by the candidate was provided to me in electronic variant.

Biographical data about the candidate

Nikolina Mihailova was born on December 2, 1980. In 2003 she obtained a Bachelor's degree in Biology at the Faculty of Biology of Sofia University "St. Kliment Ohridski", and two years later she

became a Master in Cell Biology and Pathology at the same University. In the period 2005-2008 she was a PhD student in the Department of Immunology at the Institute of Microbiology - BAS, supervisor Prof. Chavdar Vassilev, DM, PhD, DSc. In 2008 N. Mihaylova obtained PhD degree in the scientific specialty "Immunology" (PhD thesis title: "Immunomodulatory activity of new experimental IgM and IgG preparations"). From February 1, 2004 to February 1, 2005 and from February 1, 2008 to September 16, 2008 she worked as a biologist in the Department of Immunology at IMIC-BAS, immediately after which she was appointed as a research associate I degree. Since 01.01.2011 Nikolina Mihaylova has been a chief assistant in the same department. In 2007 Nikolina Mihaylova specialized for 4 months (June to September) at the INSERM Institute in Paris, where she acquired knowledge and skills in the field of flow cytometry (FACS), immunoprecipitation and cell signaling. The candidate in the competition Dr. Nikolina Mihailova is a member of the Society of Immunology at the Union of Scientists in Bulgaria and the European Federation of Immunological Societies (EFIS).

Project activity

Dr. Nikolina Mihaylova has participated in 12 scientific and educational projects financed by the National Science Fund, Ministry of Education and Science (8), the Program for Support of Young Scientists and PhD Students at the Bulgarian Academy of Sciences (1), companies (Neopharm Bulgaria EOOD - 2 projects) as well as in 2 international scientific or educational projects, supported by the Pasteur Institute in Paris, France. She is a principal investigator of two projects supported by the National Science Fund in Bulgaria (1) and the Program for Support of Young Scientists and PhD Students at BAS (1).

Teaching / Educational activity

The candidate in the competition Dr. Nikolina Mihaylova is actively involved in the training of BSc, MSc and PhD students in the Department of Immunology, IMICB-BAS. She is a consultant of a project of a PhD student / young scientist under the Program for Support of Young Scientists and Doctoral Students at BAS.

Publishing activity

Dr. Nikolina Mihaylova is the author of 36 publications, including 26 articles in scientific journals with impact factor (total IF = 93.672), 8 publications in Bulgarian (5) and international (3) journals without impact factor and 1 book chapter. The publications were cited > 250 times according to the information available in Scopus, Web of Science and Google Scholar databases (H factor = 9 according to Scopus data). She has participated in 69 scientific forums in Bulgaria and abroad with a total of 153 posters / oral presentations. A total of 23 publications (which were not included in the PhD thesis) were submitted for participation in the competition for Associate Professor, of which 19

articles in international journals with impact factor (total IF = 61.011), 2 publications in Bulgarian (1) and international (1) journals without impact factor, 1 book chapter as well as 102 citations in the databases Scopus and Web of Science.

Professional awards

The excellent professional level of Dr. Nikolina Mihailova is highly appreciated in the academic community. She has been awarded the prizes for young scientists of the Bulgarian Academy of Sciences "Prof. Marin Drinov" (2017) and "Prof. Ivan Evstratiev Geshov" (2009), the Stefan Angelov Foundation Award for the best work of a young microbiologist in Bulgaria (2008), awards for excellent performance of young scientists at international scientific forums.

Compliance of the candidate with the minimum national requirements as well as the increased criteria of BAS and additional criteria of the Institute of Microbiology – BAS for occupation of the academic position "Associate Professor"

The analysis of the materials submitted by the candidate Assistant Professor Dr Nikolina Mihaylova shows that she not only covers but significantly exceeds the national criteria for holding the academic position "Associate Professor", the increased criteria of Bulgarian Academy of Sciences, as well as specific requirements of the Stefan Angelov Institute of Microbiology - BAS. The data are summarized in Tables 1 and 2.

Table 1. Minimum national requirements and the increased criteria of Bulgarian Academy of Sciences for occupation of the academic position "Associate Professor"

Groups of indicators	Indicators	Required points	Results (Points) achieved by A. Chorbanov
A	1.PhD Thesis	50	50
В	-	-	_
С	Habilitation work - scientific publications in peer reviewed journals indexed in world- famous databases with scientific information (Web of Science and Scopus)	100	185 (9 publications in total: 3 in Q1, 4 in Q2, 2 in Q3 journals)
D	Scientific	200 / 220*	262

	publications		
	Indicator 7. Scientific publications in peer reviewed journals indexed in world-famous databases with scientific information (Web of Science and Scopus).		247 (13 publications: 3 in Q1 journals, 7 in Q2 journals and 1 in Q4 journals); 2 publications in journals with SJR without IF
	Indicator 8. Published book chapter or collective monograph		15 1 Book chapter of NOVA Publisher
E	11. Citations in scientific publications, monographs, collective volumes and patents, referenced and indexed in world-famous databases with scientific information (Web of Science and Scopus).	50 / 60*	(List of 102 citations in journals indexed in the Web of Science and / or Scopus)

^{*}According to the increased criteria of Bulgarian Academy of Sciences

Table. 2. Additional requirements / criteria for occupation of scientific position "Associate Professor" at the Institute of Microbiology "Stefan Angelov" – BAS

Scientific degree or academic position	Number of publications in journals with IF, monographs, chapters of monographs, proceedings of international forums, full-text publications, patents.	Citations*	IF*	H-factor*	Additional requirements /criteria
Requirements for Associate	20 - excluding	100	20	5	Participation in 3 projects

Professor	those			<u> </u>	
	associated with the PhD thesis, in 5 of them 1 st or corresponding author				
Indicators of Assist. Prof. Nikolina Mihaylova	23 articles (first author and/or corresponding author in 6 of	102	93.672	9 (According to a	Participation in 16 projects: Principal
*for the entire	them			reference in Scopus)	investigator in 2 of them

^{*}for the entire scientific career

Main scientific directions and contributions

The professional interests of Dr. Nikolina Mihaylova are in the fields of experimental immunology and cellular / molecular mechanisms of autoimmunity and are aimed at finding innovative solutions to some of the leading medical and societal challenges of our time, including type 1 diabetes (T1DM) and other autoimmune diseases such as systemic lupus erythematosus (SLE).

The original scientific contributions of Dr. N. Mihaylova can be grouped in three areas as follows:

- 1. Selective modulation of pathological autoreactive cells (B and T lymphocytes) by proteinengineered antibodies and by monoclonal antibodies in mouse and human models of autoimmunity.
- An innovative experimental strategy for SLE therapy has been proposed, aimed at selective suppression of autoreactive B lymphocytes the approach mimics the physiological mechanisms that inhibit the activity of these cells. It is based on the development and administration of protein-engineered chimeric molecules comprising an antibody specific for an inhibitory B cell receptor and antigenic peptides conjugated to it. The effectiveness of the approach was demonstrated in three model systems of SLE; i) spontaneous mouse model (MRL / lpr mice) and developed with its help mouse SCID lupus model, allowing long-term therapy with the chimeric molecule (that is of rat origin); ii) new pristane-induced autoimmunity model in immunodeficiency (SCID) mice; iii) a humanized model based on the transfer of B lymphocytes from people with SLE to SCID mice.
- -Bispecific chimeric molecules containing a monoclonal antibody and related epitope peptides from the GAD65 molecule (glutamic acid decarboxylase, 65kDa molecular weight isoform)

were constructed – GAD65 is among the main targets of autoantibodies associated with T1DM. The ability of these chimeric molecules to reduce the number of anti-GAD65 IgG B-producing cells and to increase the percentage of apoptotic B lymphocytes in mice (C57BL / 6J) with streptozotocin-induced autoimmune diabetes has been demonstrated.

The ability of the chimeric molecule to selectively modulate the activity of GAD65-specific cells and the anti-GAD65 autoantibodies has also been proved in in vitro experiments with peripheral blood mononuclear cells from patients with T1DM.

Original data have been obtained revealing the ability of a monoclonal antibody against Annexin A1 (ANX A1), a protein thought to be involved in the regulation of the T-cell immune response, to favorably affect the autoimmune response in various models of SLE - in MRL / lpr mice that spontaneously developed SLE, pristane – induced model of SLE in SCID mice; a humanized model of SLE in SCID mice.

2. Natural biological molecules with antitumor and adjuvant properties.

A mouse model of colon cancer (based on the C-26 cell line) was established, in which the antiproliferative / antitumor properties of hemocyanins isolated from *Rapana thomasiana* (RtH) and *Helix pomatia* (HpH) were established for the first time in vivo. In experiments with BALB / c mice, it has been shown that HpH can be used as a bioadjuvant in combination with standard antigens (peptide from the hemagglutinin molecule of influenza virus, tetanus toxoid). It has first been reported that RtH and / or its subunits can be used in various immunization protocols as adjuvants or protein carriers.

3. <u>Immunomodulatory activity of immunoglobulin molecules</u>. New information has been obtained on the increased immunoreactivity of human natural polyspecific IgG in vivo (in immunodeficient SCID mice injected with human immunoglobulin preparation) in an inflammatory microenvironment. It has been found that upon contact of antibodies with heme, in concentrations lower than those released in the blood in pathological conditions, changes in their antigen-binding characteristics occur.

Personal impressions from the candidate

I have known Nikolina Mihaylova for many years in relation with participation in various scientific forums as well as our membership in the Society of Immunology at the Union of Scientists in Bulgaria. The fact that we work in neighboring institutes also contributes to our contacts. A trained specialist with great scientific expertise, with a high sense of responsibility, good organizational skills, always ready to accept new challenges and share knowledge and experience, Nikolina has always been a wonderful example for me of a person who has found her vocation and confidently goes her path.

These impressions were fully confirmed by the documents submitted in connection with the competition, which convincingly paint the image of a hard-working and purposeful scientist with high professional standards, a proven expert in the field of immunology, respected at home and abroad. I am convinced that the academic growth of Dr. Nikolina Mihaylova will open new horizons for her, which will help her to follow her personal legend, each successes will be a cause for pride for Bulgarian science and more importantly, it is a step forward in addressing biomedical and societal challenges, including undoubtedly autoimmune diseases.

Conclusion

The materials presented by Dr. Nikolina Mihaylova in connection with the competition show that she fully meets and significantly exceeds the mandatory and specific conditions and scientometric criteria for holding the academic position "Associate Professor".

With her high professionalism, excellent organizational skills and ability to work in a team, with her rich medico-biological training, diligence, perseverance and perfectionism, with her original approach to solving problems and challenges, Dr. Nikolina Mihaylova has built a well-deserved authority of a respected researcher in Bulgaria and abroad. Today, in the high-tech 21st century, it has become more than ever clear how important and necessary biomedical science is, how valuable people who have dedicated their lives to it are. Dr. Nikolina Mihaylova is without a doubt one of them. I do believe that her example will be an inspiration and courage for future generations of scientists.

This gives me reason to convincingly propose to the Scientific Jury and the esteemed Scientific Council of the Institute of Microbiology "Stefan Angelov" at BAS to choose Assistant Professor Nikolina Mihaylova Mihaylova, MSc, PhD, as ASSOCIATE PROFESSOR in the professional field 4.3 Biological Sciences (specialty "Immunology"), announced for the needs of the Department of Immunology at the same Institute.

07.07.2021.

Sofia

Prof. Ra

exandrova, PhD