

OPINION

of Prof. Dr. Dimitar Stefanov Kadiysky, Doctor of Medical Sciences, Institute of Experimental Morphology, Pathology and Anthropology with Museum (IEMPAM) at BAS, Acad. G. Bonchev St., bl. 25, 1113 Sofia;

member of the Scientific Jury of the competition for the academic position of *associate professor* under Order No. RD 15-62 of 26.05.2023 of the Director of IEMPAM.

Regarding: Conducting a competition for the academic position "associate professor" for the needs of the Pathology Section at IEMPAM, in the scientific specialty "Immunology" (01.06.23), professional direction 4.3 "Biological Sciences", announced in the State Gazette - issue 38, p. 79, dated 28.04.2023, on the proposal and decision of the Scientific Council of IEMPAM.

In the announced competition, the candidacy of only one participant was received - Rositsa Svetolik Milcheva, chief assistant in the Pathology Section at IEMPAM at the Bulgarian Academy of Sciences. The materials submitted by the candidate (with me in electronic form) are in full compliance with the national normative requirements for occupying academic positions and are in accordance with the specific norms of the regulations of the BAS and IEMPAM. All documents are available in a well-arranged form.

I. Career profile of the candidate

Chief assistant Rositsa Svetolik Milcheva, doctor, in the period 1997 - 2002 graduated from Sofia University "St. Kliment Ohridski", Faculty of Biology, as a master's degree in Molecular Biology, together with a specialization in Clinical Chemistry, for which she received a diploma A-2002 of SU No. 160673. From December 2007 to August 2011, she was a doctoral student in Bratislava, Slovak Republic - Comenius University, Faculty of Medicine, Department of Pathology. There, after defending a dissertation (thesis), she received the educational and scientific degree "doctor" with code 7.1.21 pathology and forensic medicine (diploma UK*4410). The topic of her dissertation, defended on 08/24/2011, is: "Mechanisms of apoptosis in striated muscle fiber after invasion by *Trichinella spiralis*" (in English), with certificate of originality number 9b10f655-274f-4ce0-aae9-43dB93e7eff by Slovak standards.

From 2002 to the present, the participant in the competition has successively held academic positions at IEMPAM: specialist (October 2002 - January 2005), from January 2005 to June 2010 research assistant, assistant from June 2010 to January 2014. Since 2014, she has been the chief assistant at IEMPAM.

The scientific and professional development of ch. assistant Rositsa Milcheva is associated with specializations in various programs abroad: specialization at the Faculty of Medicine at Comenius University in Bratislava, Slovak Republic; studying at the Imperial College in London, Great Britain; specialization at the Institute of Biological, Environmental and Agricultural Sciences at the University of Wales in Aberystwyth, Great Britain; specialization at Institute of Molecular Biosciences at Karl Franz University in Graz, Austria.

Her development as a scientist includes management and participation in research activities on various projects: management of 2 projects and executor in a third, financed by the "Scientific Research" Fund; participation in three projects financed from other sources. As of the date of the competition, she is a project manager with the Slovak Academy of Sciences under the program "International cooperation within the framework of interacademic contracts and agreements".

II. General description of the submitted materials for the competition

The detailed documentation presents the candidate as a promising scientist with indisputable results of successful academic growth. A significant part of the scientific and career profile of ch. assistant Rositsa Milcheva is related to *the immunological reading* of her results on the morphology, genetics, biochemistry and function of the so-called *supporting* cell, created during direct invasion of the parasite *Trichinella spiralis* in the striated muscle tissue. The very term "*support cell*" was successfully proposed by Rositsa Milcheva in the Bulgarian scientific terminology and is equivalent to the well-established English term "nurse cell".

During his scientific growth ch. assistant Rositsa Milcheva has published 29 scientific papers. A significant part of them (22) have been published in international refereed and indexed editions (visible in Web of Science and Scopus). There are 21 of them with an impact factor or impact rank. In 12 publications, Rositsa Milcheva is the first author. Some of these publications are in really valuable scientific publications such as *Acta histochemica*, *Parasitology research*, *Biologia*, etc. She has an h-index of 5 and has found to date 74 citations of its scientific output. 19 are submitted for participation in the competition. She is a participant in 12 national and 10 international scientific forums.

The scientometrics of the candidate's previous research activity is presented in a separate panel, from which it is evident that she fully covers and in some indicators exceeds the requirements of the Regulations for the implementation of the Law for Development of Academic Staff (LDAS) in the Republic of Bulgaria, adopted with Ministry council decree 122/29.06.2018 and in force from 06.07. 2018 with its later additions, effective at the time of the announcement of the competition in the State Gazette. The scientometric requirements and conditions stemming from the Rules of the BAS for the application of LDAS in the Republic of Bulgaria and, of course, the Rules of the IEMPAM for occupying academic positions are fully met.

III. Evaluation of the candidate's scientific works

In the process of her professional growth, Rositsa Milcheva has mastered and implemented a wide range of scientific approaches and skills: various research techniques, biostatistical analyzes of the obtained data, author's design of primers with functioning efficiency and specificity. The wide range of research approaches - lectin and immunohistochemistry, one- and two-dimensional electrophoretic techniques, western and lectin affinity-blot, flow cytometry, yeast and *E. coli* cultivation, cell death analysis (Annexin V/PI and TUNEL tests), real time PCR, gene expression analysis, etc. contributes to the quality of scientific results achieved.

Since a detailed assessment of the candidate's scientific activity will be presented by the reviewers of this competition, I will briefly touch on her original scientific and scientific-applied contributions including:

- detailed screening of glycosylation changes in the parasite *Trichinella spiralis* during the different stages of nematode development. This research has relevance and possible application in therapeutic approaches to autoimmune diseases, allergies and malignancies.
- obtaining new data concerning the mechanisms of apoptosis in the adaptation of *Trichinella spiralis* in the tissues by building an effective niche of residence in the striated muscle tissue. The results of these studies are relevant in explaining the suppression of the infected host's immune response to the parasite.
- establishing the specificity of apoptosis mechanisms during the intestinal phase of infection with *Trichinella spiralis*.
- receiving clear methodical contributions – e.g. promoting the applicability of various alcohol-based fixatives and their introduction to histology and molecular biology in order to optimally preserve morphology, protein immunoreactivity and RNA integrity in fixed tissues.
- obtaining results for the content of free, lipid-bound and protein-bound sialic acid in the serum during different phases after infection with *Trichinella spiralis*, related to the context of the non-specific immune response of the host.
- registration of the nuclear localization of proteins in striated muscle cells after invasion with *Trichinella spiralis*. This contribution is directly related to the process of transformation of an invaded striated muscle cell into a "support cell" by *T. spiralis*.

A separate trend of the candidate's studies, fully related to practice, is the discovery of the impact of mycotoxins Fumonisin B1 (FB1) and deoxynivalenol (DON) on the immune system, including the establishment of a cytotoxic effect on cell lines of different origins.

A general overview of the topics of the established scientific projects on which the candidate worked and the topic of her dissertation work shows her interest in the practical problems of modern immunobiology, immunochemistry and immunomorphology, which represent a significant part of the large biomedical scientific direction.

IV. Recommendations and critical notes

I highly recommend continuing the research activity, attracting scientists and doctoral students and creating a working team around the interesting topic incl. to study the cytokine profile in different phases of *Trichinella spiralis* infection.

V. Overall Assessment of Conformity

The applicant's compliance with the mandatory conditions and the mandatory quantitative criteria in relation to the scientometric indicators, according to the LDAS in the Republic of Bulgaria and the relevant regulations for occupying academic positions, is complete.

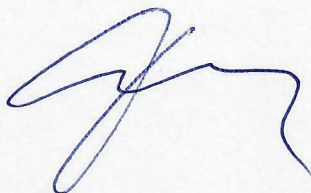
VI. Conclusion

Ch. assistant Rositsa Milcheva, doctor, participated in the competition for "associate professor" with a significant volume of scientific activity. In her research work, she used a complex of classic and modern methods for immunological, molecular-genetic and cell-biological research. She is a competent and highly qualified researcher, a fair and tolerant colleague. She works excellently both independently and in a team with specialists from IEMPAM and from university research laboratories in Slovakia.

In summary of the above, I believe that ch. assistant Rositsa Milcheva fully meets the requirements of the LDAS in the Republic of Bulgaria, the Regulations for its application and the relevant requirements of the BAS and IEMPAM for awarding the scientific title "associate professor". The complex evaluation of her documents gives me the reason with full conviction to propose to the respected Scientific Jury to make a positive decision to the Scientific Council of IEMPAM chief assistant Rositsa Milcheva to be elected to the academic position of assistant professor in "immunology".

Prepared the opinion:

Signature:



16.08.2023

Prof. Dr. Dimitar Kadiysky, PhD