OPINION

by Prof. Rayko Dimitrov Peshev, Ph.D. Section “Epizootology and Infectious Diseases in Animals” in the National Veterinary Research Institute of the City of Sofia for the announced competition in the State Gazette No.93 of 26.11.2019 for the occupation of the academic position “Associate Professor” in the field of higher education 4. Natural sciences, mathematics and computer science, professional field 4.3 Biological Sciences (Virology).

In connection with the announced competition from the Stephan Angeloff Institute of Microbiology at the Bulgarian Academy of Sciences No.93 dated November 26, 2019 for the occupation of the academic position of Associate Professor in the field of higher education 4. Natural sciences, mathematics and informatics, professional field 4.3 Biological Sciences (Virology) documents have been submitted by a single candidate Assist. Prof. Ivanka Nikolova Nikolova, Department of Virology, Institute of Microbiology "Stephan Angeloff", BAS within the legally established period. The candidate has submitted the necessary documents for the competition - list of scientific papers, list of participation in scientific conferences, list of participation in scientific projects, list of citations, reference for research work, reference for fulfillment of additional requirements of the Institute of Microbiology at BAS, scientific contribution reference, reference for meeting the minimum requirements according to ZRARB.

Scientific publication activities

In her dissertation, Dr. Nikolova studies the emergence of resistant and dependent mutants of the Coxsackie B1 virus to the picornaviral inhibitor disoxaril and 3 scientific reports have been published in connection with the dissertation.

A list of 25 scientific papers is presented, most of them reflecting the results associated with studies on experimental chemotherapy of viral infections. Dr. Nikolova studies the phenomenon of drug resistance in enterovirus infections (the main reason for the lack of clinically effective chemotherapeutics for the treatment of enterovirus infections), including the phenotypic characteristics of the treated viruses and the molecular genetic basis of resistance. A novel approach is described for combined in vivo administration of antiviral drugs, not simultaneous but sequential, alternative administration (CAA), of triple combinations of enterovirus replication inhibitors with different mechanism of action (directed against VP1 - disoxaryl, pleconaryl), 2C protein (guanidine HCl) and the cell factor phosphatidylinositol-4-kinase IIIß (oxoglucin, MDL-860). Screening was conducted to detect promising inhibitors for the replication of enteroviruses, herpes viruses, adenoviruses and respiratory syncytial virus, and the antiviral activity of substances of natural or synthetic origin was disclosed. Genomic changes in cervical precancerous lesions and tumors induced by different types of human papillomaviruses in Bulgarian patients have been performed by microarray CGH analysis.

The contributions from these studies can be related to the following trends: the development of drug resistance to an in vivo model WIN compound in neurotropic Coxsackie B viral infection in mice. To characterize the viral drug mutants, the phenotypic markers of the virus have been identified, which change after treatment with the various antiviral agents, such as MIC_{50} value, size and shape of agar plates, resistance at 50°C, pathogenicity in mice. The molecular bases of drug resistance were determined to determine differences after sequencing of wild Coxsackie B virus and the resulting disoxaryl mutants. One very important contribution is the invention and subsequent development of a treatment course under the scheme of sequential alternative administration of a triple combination

of enterovirus inhibitors, which is a novelty in the chemotherapy of viral infections. In vitro synthesis and screening for anti-enterovirus activity (against PV1, CVB1 and CVB3) of over 70 new analogues of MDL-860 (a key compound for the construction of a triple anti-enterovirus combination) revealed that 7 of them are characterized by their extremely high in vitro activity.

Dr. Nikolova has participated in presentations of the results of her research at 36 scientific conferences, symposia and congresses with Bulgarian and international participation.

The total number of citations (excluding self-citations) is 133, which indicates that the results obtained by the candidate are valuable for science and practice and are appreciated by our and foreign researchers. The total impact factor is 26.842 and the H-factor is 3.

Dr. Nikolova is a contractor and participant in a total of 9 scientific projects, of which three international projects, four projects funded by the Research Fund and two projects funded by BAS, which contributed to part of the financial support for the implementation of the projects.

From 2015 to 2019, Dr. Nikolova conducted undergraduate studies at the New Bulgarian University and the Faculty of Physics at the Sofia University on Viral and Bacterial Infections of the Eye.

Compliance with national minimum requirements

From the reference for meeting the national minimum requirements and the criteria specific to the Institute of Microbiology, I have found that:

Group A - holds a dissertation for the doctorate degree - 50 points.

According to indicator B-publications in abstracted and indexed databases with scientific information, a total of 25, with the required 20. (excluding those for the Doctor) in five of them she is the first author, and is also involved in writing a chapter of a book, which total 102 points.

In indicator D there are 219 points with 200 required.

There are 133 citations or 266 points in the E indicator, with 50 points needed.

Impact factor at the required 20 it exceeds it and has 26.842.

She has participated in 9 international and national scientific projects with 3 required participations. She has taught students bacterial and viral infections.

The information provided shows that Dr. Nikolova fulfills the minimum national and University Institute of Microbiology requirements for occupying the academic position of Associate Professor.

Unfortunately, the minimum national requirements are not sufficiently objective and should probably be revised and refined because they lack an assessment of the lectures of the applicants.

Conclusion

The information provided by Dr. Ivanka Nikolova Nikolova on the research and application activity and the results achieved in the field of antiviral therapy give me reason to conclude that it meets the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria, the Implementing Regulations his and the Internal Regulations of the Institute of Microbiology of BAS. This allows me to recommend that the members of the Scientific Jury and the members of the Scientific Council of the Institute of Microbiology vote positively for the award of the academic

position of Associate Professor to Dr. Ivanka Nikolova Nikolova in higher education 4. Natural sciences, mathematics and computer science, professional field 4.3 Biological Sciences (Virology).

Prof. Raiko Peshev