

## REVIEW

by Assoc. Prof. Lyubka Yordanova Dumanova - Yazadzhieva, PhD, Institute of Microbiology Stephan Angeloff at BAS, member of the Scientific Jury based on a decision of the Scientific Council of IMICB (Minutes No. 12 / 28.11.2019 and 13 / 17.12.2019) and Order No. 130 / 23.12.2019 of the Director of IMICB, selected for reviewing the first meeting of the Scientific Jury, held on 01/28/2020 at 11.30 am, of the materials submitted for the competition to occupy the academic position of Assistant Professor for the needs of the Department of Virology of the Institute of Microbiology "Stephan Angeloff" at BAS in the field of higher education 4. Natural sciences, mathematics and informatics in the professional field 4.3. Biological Sciences in the scientific specialty "Virology"

## LEGAL LAW OF THE ANNOUNCED COMPETITION

The competition was announced in the State Gazette (SG) issue 93 of November 26, 2019, as well as on the website of the Institute of Microbiology at the Bulgarian Academy of Sciences (IMikB) for one place in the scientific specialty "Virology". During the two-month period from the date of the announcement of the competition in the State Gazette, documents were submitted by a single candidate – Assist. Prof. Dr. Ivanka Nikolova Nikolova. The candidate was admitted to the competition by the Commission, determined by order No. I - 12 / 20.01.2020 of the IMICB Director. After reviewing the set of documents submitted, the Commission confirmed the regularity and availability of all required documents. In protocol of 27.01.2020, the Commission declared that the candidate was in compliance and that the procedure for selecting Assist. Prof. Dr. Ivanka Nikolova Nikolova for the academic position of Associated Professor.

On the basis of these data, I believe that the competition meets the requirements for occupation of the academic position "Associated Professor" in accordance with the Law on the Development of Academic Staff in the Republic of Bulgaria, the Regulations thereto, as well as the Regulations on the conditions and the order for acquiring the academic degrees and holding academic positions at ImikB - BAS.

## BIOGRAPHICAL INFORMATION ABOUT THE APPLICANT

Dr. Ivanka Nikolova was born on 12.11.1972 in Burgas. He received his secondary education at the Russian Language School in Burgas in 1990. In 1995 he completed his higher education, majoring in biology and chemistry at the Faculty of Biology (BF) of Sofia University "St. Kliment Ohridski "(Sofia University). In 2004, she obtained her Doctorate degree in Virology from the Department of Virology at the Institute of Microbiology at the Department of Virology at the Institute of Microbiology, based on a Ph.D. Stephan Angeloff "at the Bulgarian Academy of Sciences (IMikB-BAS), headed by Academician Angel S. Galabov.

She has received all her professional experience at IMikB-BAS, having worked as a biologist-specialist in the Microbial Genetics Section for 4 years, and after defending her PhD since 2001 when she has been working as a specialist, research assistant, Assistant Professor, head of laboratory "Experimental chemotherapy for enterovirus infections" at the Department of Virology, of which the laboratory has been headed since 2016.

During the period 2008-2010 she conducts exercises in Molecular Virology at the Sofia University, from 2014 to the present and from 2016 to the present he conducts respectively exercises in Virology at the New Bulgarian University and lectures on bacterial and viral infections of the eye at the Faculty of Physics (FF) of SU.

Since 2012 she has been a member of the Union of the Scientist in Bulgaria (USB), section "Microbiology", and since 2015 she is secretary of the National Virology Seminar at IMICB and secretary of the Foundation "Acad. Prof. Dr. Stephan Angeloff".

#### DESCRIPTION, GROUPING AND REFERENCE FROM THE REVIEW OF THE CANDIDATE DOCUMENTS

Dr. Ivanka Nikolova participates in the current Docent Contest with a total of 25 titles according to the annexes to the List of Publications. A separate list of 36 abstracts from participation in scientific events with reports and posters is presented. These headings can be grouped as follows:

1. Abstract of dissertation for awarding educational and scientific degree "Doctor" -1 issue;
2. Scientific publications for the doctoral dissertation - 3;
3. Scientific publications outside the doctoral dissertation - 22 issues, of which:
  - a / scientific publications related to the main direction of the Virology Competition - 21;
  - b / publications in foreign magazines Impact factor journals - 12;
  - c / book chapters - 2;
  - d / scientific articles in full text in collections of national and international forums - 4;
4. Attendance at conferences - 36 in total (25 posters and 11 papers), of which:
  - a / at the international level - 33;
  - b / at national level - 3;
5. Total impact factor - 26,842;
6. H-factor - 3;
7. Other materials:
  - Habilitation report (Reference for original scientific contributions);
  - List of cited references -133 total number (without quotes);
  - List of participation in project development - 9 issues, 3 of which are international, four funded by the NSF at the Ministry of Education and Science and two funded by the Bulgarian Academy of Sciences;
  - 9 CDs;
  - references (job notes) for teaching employment;
  - references to the Minimum National Requirements (MNEs) under the ZRARB and the additional requirements in the IMICB Regulations;

Subject to review are materials other than those referred to in Items 1 and 2, the scientific value and contributions of which have been evaluated by the reviewers of the doctoral dissertation by the Specialized Scientific Council of the Higher Attestation Commission where Ivanka Nikolova has defended her dissertation ( 12.01.2004).

## ANALYSIS OF SCIENTIFIC LABOR AND EVALUATION OF CONTRIBUTIONS

The studies conducted by the candidate according to the attached habilitation report address issues in three main areas:

1. Experimental work on chemotherapy for enterovirus infections.
2. Broad-based screening aimed at detecting promising inhibitors of the replication of enteroviruses, herpes viruses, adenoviruses and respiratory syncytial virus.
3. Detection, genotyping and genetic analysis of various DNA viruses (cytomegalovirus and papilloma viruses) in samples from Bulgarian patients.

The first and most comprehensive section, Experimental Work on Chemotherapy for Enterovirus Infections, includes the bulk of scientific work focused on experimental work on the search for new approaches to the effective chemotherapy of enterovirus infections to overcome the drug resistance phenomenon.

This section includes 12 articles, 9 of which are reviewed # 1,5,6, 7, 9, 10, 14, 19, 20. The candidate builds on the results of her dissertation, where for the first time they reveal why treatment has failed with one of the most effective inhibitors of enterovirus-disoxaril. It continues to explore other promising enterovirus inhibitors, with an important step in the introduction of phenotypic markers to characterize resistant and dependent viral drug mutants (Article 5).

Another series of publications (Nos. 6,7,9,10,8) treats the testing of the combined effects of selective enterovirus replication inhibitors with different mechanisms of action in studies of anti-enterovirus agents for the first time introduced a sequential scheme alternative introduction (CAA). The contribution here is not only that the CAA course is a novelty in the chemotherapy of viral infections in general, but also the result that this regimen prevents the development of drug resistance, thereby ensuring clear antiviral activity.

The following is scientific work No. 20 on the identification of RNA mutations and amino acid substitutions in the VP3 region by genomic analysis of viral isolates taken from mice treated with a CCA triple combination inhibitor - RMO system, in which there is a lack of resistance and increased sensitivity to antiviral agents.

Two other publications (No. 14,19) reveal the success of the in vitro synthesis and subsequent screening research for the antiviral activity of over 70 novel analogues of one of the key compounds for the construction of the concept of a triple-enterovirus combination. After selection, several leading compounds with a strong inhibitory effect on the replication of Coxsackie B1 virus were selected.

The second tendency, Broadband Screening, aimed at detecting promising inhibitors of the replication of enteroviruses, herpes viruses, adenoviruses and respiratory syncytial virus, includes publications Nos. 8, 15, 17, 18 and 21 of the inhibition of various viral infections by substances of both synthetic and natural origin. Screening studies include current viral agents from different taxonomic groups of viruses. Substances of natural and synthetic origin are also very diverse - organosilicones, merocyanins and salts of violoric acid, monoterpenic alcohol geraniol, elagitanins, plant extracts. Research in this area reveals the antiviral potential of the various substances tested.

The third tendency "Detection, genotyping and genetic analysis of various DNA viruses (cytomegalovirus and papillomaviruses) in samples from Bulgarian patients" refers to three articles - Nos. 12, 13 and 14. The development in Article 13 is original since it was first introduced. Genomic changes in cervical precancerous lesions and tumors induced by different types of human papillomaviruses in Bulgarian patients by microchip CGH analysis were investigated.

The topicality and the interesting results of the research are well-regarded by the scientific community, as I have already mentioned the citations are 133 in 7 publications, IF is 26,842 and 36 participated in national and international conferences.

The analysis of the works according to the candidate's participation shows that she is the leading author in 5 of the attached publications, in another five of them is the second author, and in 12 - the third and the next, from which she can see her contribution, expressed in a clear and professional profile of a specialist in the field of enterovirus infection chemotherapy and screening aimed at detecting promising inhibitors of replication of various viruses, as well as methodological training specific to this field. Methods for assessing antiviral activity are mainly virologic - determination of cytotoxicity, inhibition of plaque formation, inhibition of virus-induced cytopathic effect, phenotypic characterization of mutants under the action of active substances in increasing concentrations; molecular biological methods - electrophoretic, polymerase-chain reaction, sequencing, etc.

#### TEACHING ACTIVITIES:

In the period 2014 - 2019, Dr. Nikolova is a part-time lecturer at the New Bulgarian University and has taken courses in the programs at the Department of Natural Sciences, giving a total of 28 lectures in the field of Virology during this period and there are 150 h and exercises on Genetics, Virology, Infectious Diseases and Immune Response. She leads the courses on Viral and Bacterial Infections of the Eye at the Faculty of Physics at Sofia University "St. Kliment Ohridski ". For the period 2015-2019, the employment of Dr. Nikolova totaled 270 hours of lectures in both courses.

This teaching activity and commitment presents Dr. Nikolova not only as a scientist, but also as a teacher who educates young colleagues successfully and thus contributes to the creation of new Virology staff.

#### ANALYSIS OF THE REFERENCE TO COMPLY WITH THE MINIMUM NATIONAL REQUIREMENTS AS TO THE ADDITIONAL IMICB CRITERIA

The reference for the fulfillment of the minimum national requirements, as well as the additional criteria of IMICB for the growth of the academic staff at the Institute, shows that Dr. Nikolova fulfills these requirements and criteria, namely:

Indicator A - holds a dissertation for the doctorate degree - 50 points in total. Corresponds.

Indicator B - Scientific publications in publications, referenced and indexed in a scientific information database - 102 points in total.

Indicator C - a total of 217 points is indicated, with a required 200. The candidate has omitted to her detriment the article No. 7 of 2018 in *Biointerface Research in Applied Chemistry*, 8 (1), 3053-3059., Which has Q3 - 15 tons ., which can be added to the total score for this metric. Corresponds.

Indicator D - a total of 266 points for 133 citations (without auto-citations) with 50 points needed. Corresponds.

For the additional criteria, it covers them, exceeding the required number of articles, namely 25, with the required 20. (excluding those for "doctor"); 5 of them are the first author; exceeds the required IF (26,842); participates in 9 projects, only one does not cover the H-factor.

Nikolova has good language and computer skills.

#### PERSONAL IMPRESSIONS FROM THE CANDIDATE

I have known Ivanka Nikolova since she was working on her thesis, ie. my personal impressions are long lasting. She has always left me with the impression of a correct and responsive colleague, an organized researcher with extensive experience and skill in planning and conducting experiments in the laboratory, a very good and sought-after teacher. I recommend an even more productive publication activity in order to outline the personal appearance and motivation of a scientist with a future in Virology.

#### CONCLUSION

The materials submitted for the competition by Ivanka Nikolova fully comply with the requirements of the ZRASRB and its Regulations, the Rules of IMiKB-BAS for the occupation of the academic position of "Associate Professor". All procedures were followed in the course of the announced competition.

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

Analyzing the materials of the competition, I believe that Ivanka Nikolova is a highly qualified scientist, with sufficient scientific production in the important scientific fields, professionally developed by her, excellent professional biography and active training activity. Nikolova has the experience and knowledge of successful research in the field of virology, enterovirus chemotherapy, study of the phenomenon of drug resistance, search for promising inhibitors of viral replication, etc., as well as knowledge of specific methodological approaches. These qualities of an intelligent and organized researcher, able to work independently, to educate students, open up good opportunities for her future growth in her chosen scientific field. Research on modern antiviral chemotherapy is important, as enterovirus infections affect billions of individuals, leading to hundreds of thousands hospitalized annually. In addition to viral therapy, one can also think of possible drug prophylaxis with any of the substances studied.

Therefore, I give my positive opinion and believe that the only candidate in the competition is fully deserving of being awarded the scientific title of the announced competition for Associate Professor. Based on this positive assessment, I recommend that the Scientific Jury make a proposal to the Scientific Board of IMICB for the election of Dr. Ivanka Nikolova Nikolova to the academic position of Associated Professor in the Virology Department of IMICB Higher Education Area 4. Natural Sciences, Mathematics and computer science in the professional field 4.3. Biological Sciences in the scientific specialty "Virology".

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