



To  
the chairman of the scientific jury,  
determined by order № rd-09-48, 27.07.21.  
of the Director of IEMPAM, BAS

Attached I present: Review  
in a competition for the academic position of "associate professor"  
in the scientific specialty "Virology"  
announced for the needs of IEMPAM, BAS, section "Pathology"  
in sg, no. 59 / 16.07.2021

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The review is compiled in accordance with the requirements of LDACRB and section III / section IV  
of RILDACRB - conditions and procedure for holding the academic position of "Associate professor"  
/ "Professor"

## REVIEW

in a competition for the academic position of "Associate professor" in the professional field 4.3.  
Biological sciences, scientific specialty: "Virology" sh. 06/01/13,  
announced in sg, no. 59 / 16.07.2021, for the needs of the section "Pathology", IEMPAM - BAS

by Prof. Krassimira Todorova-Hayrabedyan, PhD, DSc  
Head of the laboratory of reproductive omics technologies,  
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### **I. Analysis of the candidate's career profile.**

Ch. Assistant professor Ani Krasimirova Georgieva is the only candidate in the competition. She has completed a master's program in "molecular biology" with a specialization in "animal and human physiology" at Sofia University "St. Kliment Ohridski" in 2000. In 2002 she has appointed as a laboratory assistant at the Institute of experimental morphology, pathology and anthropology with a museum, BAS. In the period 2004 - 2007 she was a phd student in full-time education at IEMPAM. Since 2007 until 2011 she was appointed as a specialist - molecular biologist, and since 2011 until 2015 she has held the academic position of assistant. In 2014 Ani Georgieva has defended her dissertation on "*in vitro* and *in ovo* models of chemical and reovirus-induced carcinogenesis". In 2016 dr. Ani Georgieva has held the academic position of "chief assistant" at IEMPAM.

### **II. General description of the submitted materials in the competition.**

The materials presented in the competition are well arranged and reflect the requirements of the law and the regulations for the implementation of the law for the development of the academic staff in the republic of Bulgaria, as the materials are presented in both paper and electronic media. The overall history and production of Ch. assistant professor A. Georgieva, both through a CV, lists of publications and citations, and through the submitted scientific contributions, and reference-declaration for implementation of minimum national requirements and the requirements of BAS for participation in a competition for "associate professor", in area 4 natural sciences, mathematics and informatics professional field 4.3. biological sciences. The presented data show, according to a preliminary assessment, coverage of the minimum scientometric and other criteria of the law, as well as of the rules of BAS for development of the academic staff, which allows subsequent detailed evaluation of the application.

### **III. Evaluation of the candidate's scientific works for the overall academic development.**

#### *General characteristics of the scientific production and publication activity;*

To participate in the competition are presented 1 abstract of a dissertation and 35 scientific articles, all published in English, 21 of which have an impact factor or rank. Of the referenced and peer-reviewed publications, 6 are in journals with rank Q1; 4 are of rank Q2; 8 are of rank Q3 and 3 are of rank Q4. The publications are in a number of prestigious journals such as Biomedicines, International journal of biological macromolecules, Journal of ethnopharmacology and others.

#### *Scientific activity - dissemination and application of the scientific and practical achievements of the candidate among the scientific community*

The scientific production is very good and is well reflected in the scientific community through citations and through its presentation in a number of scientific forums. Data for participation in 74 scientific forums in the country and abroad are presented, with oral reports and posters.

Data for 116 citations from 14 literature sources, in which dr. Georgieva is the author, are presented. In the analytical tools of the information system Scopus Ch. assistant professor A. Georgieva is evaluated with h-index 6.

The high scientific activity of dr. A. Georgieva in the last 5 years is emphasized, which is demonstrated by the publication of over half of the articles with which she applied for the competition. Also, these articles have an impact factor and rank.

Ch. assistant professor A. Georgieva is also very successful in the field of project financing, having participated in a total of 14 projects, mainly funded by the National Science Fund.

#### *scientific and creative achievements (scientific authority);*

The developments of Ch. assistant professor A. Georgieva are in 3 thematic areas: Virology, Oncovirology and Experimental oncology, and in each area there are several areas. Briefly, contributions can be synthesized:

1. It is known that there is a worldwide problem of declining bee populations. The reasons are different (plant uniformity, viruses, pesticides, etc.). This leads to a serious ecological crisis related to the impossibility of pollination in plants. The results obtained from the scientific developments of dr. Ani Georgieva show the origin and distribution of bees in Bulgaria. The most significant contributions are related to the detection of 6 different viruses that cause serious damage (wing deformation, paralysis) to honey bees. The strains of the studied viruses were established by molecular-biological techniques (sequencing), and their origin and distribution were established by phylogenetic analysis. The genetic similarity of the Bulgarian strains with other strains from different regions of the world has also been proven. The nucleotide sequences are deposited in Gen bank under certain code numbers.

2. One of the great contributions of assistant professor Ani Georgieva in the field of oncovirology is her participation in the development of a permanent cell line from Grafi's virus-induced myeloid

tumor in a hamster. The contribution is related to the possibility of testing different and a large number of anti-tumor drugs, determining optimal doses and effectiveness of the natural or synthetic substances used.

3. Contributions in the field of experimental oncology shall relate to the assessment of the potential risks to human and animal health exposed to the fungicide mancozeb. A concentration-dependent cytotoxic effect of the studied fungicide on primary cultures of embryonic cells of golden hamster and balb/c 3T3 cell line was established. In an *in ovo* carcinogenicity test, the formation of liver preneoplastic lesions was found only at doses causing high embryonic mortality and severe toxic organ damage.

4. The mechanisms of cytotoxic action of the mycotoxin fumonisin b1 in cell cultures of embryonic cells from birds and mammals have been studied. The studied mycotoxin was found to cause a concentration-dependent decrease in cell viability. Cytomorphological studies of cells cultured in the presence of fumonisin b1 show pronounced apoptotic and necrotic changes.

5. Derivatives of aminophosphonic acid with the possibility of application in medicine and pharmacy as new antiviral and antitumor drugs have been studied. Their structural similarity to the  $\alpha$ -amino acids that make up the proteins of living organisms and their characteristic lipophilicity allow them to easily penetrate the cell and nuclear membranes. The studied newly synthesized compounds are characterized by low cytotoxicity, do not show genotoxic and carcinogenic effects when tested in *in ovo* model systems.

6. Newly synthesized anthracene-containing  $\alpha$ -aminophosphonates and their derivatives in a panel of human tumor cell lines - a model for cervical adenocarcinoma, colorectal adenocarcinoma, invasive mammary carcinoma adenocarcinoma, hepatocellular carcinoma and bladder carcinoma, as well as in an Ehrlich carcinoma cell line in mice were studied as potential for use in anti-tumor therapy. Strong cytotoxic and antiproliferative activity of the tested compounds was found.

7. The effect of alkylphosphocholine erufosine as a promising antitumor agent and the possibility of its use as part of complex chemotherapy has been established. Erufosine has been shown to inhibit graft tumor cell proliferation, induce cytoskeletal reorganization, and apoptosis. In addition, the results of *in vivo* studies showed a protective antitumor effect of erufosine administered alone or in combination with the conventional cytostatic doxorubicin in hamsters with experimental graft's myeloid tumor. The applied experimental antitumor therapy leads to a decrease in the biometric parameters transplantability, tumor volume and mortality, as well as to a decrease in metastatic activity and prolongation of the average survival time.

8. Significant developments have been carried out in the search for an opportunity to overcome the shortcomings of biologically active substances of natural origin with proven anti-tumor properties, but with chemical instability and low bioavailability, which leads to limited therapeutic potential. The inclusion of substances in a polymer matrix is a contribution of the conducted experiments. A model of cervical carcinoma was used, with increased cytotoxic and anti-proliferative effects; apoptosis is induced in tumor cells.

9. Through the use of commercial cell lines, such as model systems for cervical adenocarcinoma (Hela), adenocarcinoma of the colon (HT-29) and breast cancer (MCF-7), studies have been performed to establish the anti-tumor properties of non-steroidal anti-inflammatory drugs already used in practice. Induction of apoptosis, inhibition of adhesion and migration of tumor cells has been established, which is essential for overcoming metastasis.

10. Hemocyanins that have been used to treat human colorectal cancer cells (HT-29) have been studied with the potential to develop anti-tumor agents. Glycoproteins were isolated from arthropods and mollusks and had antitumor effects expressed by induction of apoptosis in the studied cancer cells.

In addition to the specifics from a scientific point of view of the contributions listed in the works of dr. Ani Georgieva, it should be noted the applied nature of the research and their implementation in practice.

1. The introduction of *in ovo* model systems is a good approach to assess the genotoxic and carcinogenic potential of various chemical compounds, and is also in line with the ethical and moral aspects of research related to the use of experimental animals. It is known that more than 1 million experimental animals are killed each year in laboratories around the world. These tests are one of the alternatives for future work.

2. The implementation and maintenance of cell lines (primary and commercial) can also be noted as an applied contribution.

3. The application of molecular biological technology to detect viruses in bees is also not only a scientific but also an applied achievement that could contribute to solving an important problem of agricultural, economic and environmental importance.

#### **IV. Evaluation of the monographic work or equivalent publications submitted for participation in the competition for "associate professor" by the candidate.**

Ch. assistant professor A. Georgieva presented 4 publications with Q1, which correspond in weight to monographic work. My personal opinion is in favor of the application of original scientific developments, because modern trends in scientometrics give weight to original research.

#### **V. General assessment of the applicant's compliance with the mandatory conditions and the mandatory quantitative criteria and scientometric indicators.**

The procedure presents scientometric data according to LDACRB and RILDACRB, as well as the minimum criteria of BAS in area 4. Natural sciences, mathematics and informatics professional field 4.3. Biological sciences (Virology), in sub-categories as follows:

1. By group of indicators "A" - 1. successfully defended dissertation for awarding "doctor" - presented abstract **(50 of 50 points)**
2. By group of indicators "B" - habilitation work or scientific publications in publications - publications with rank Q1 - 4 are presented. **(100 out of 100 points)**
3. By group of indicators "D" - scientific publication in publications that are referenced and indexed in world-famous databases - 17 publications (with rank Q1 - 1 pc., with Q2 - 5 pcs., with Q3 - 8 pcs. and with Q4 - 3 pcs.) **(281 points out of 220 points)**
4. By group of indicators "E" - citations in scientific publications, monographs, collective volumes and patents, referenced and indexed in world-famous databases with scientific information - 93 citations **(186 points out of 60 points)**

The current application exceeds the required points according to the criteria (617 points out of the required 430 points).

## VI. Conclusion

This application fully meets the mandatory and specific conditions and scientometric criteria - for the academic position of "Associate professor". Ch. assistant professor Ani Georgieva has 63 scientific papers, 74 participations in scientific forums and 116 citations. For the competition she presented 35 publications and abstracts, and 93 citations. Most publications have an impact factor and rank. She has been a project manager and has participated in numerous projects.

In conclusion, I strongly vote "YES" and recommend to the scientific jury for this competition the award of the academic position of "Associate professor" to dr. Ani Georgieva, believing that her professional qualities and long-term achievements make her suitable as a leading researcher and future research supervisor for graduates and PhD students.

Sofia,  
10.11.2021

Reviewer:



/ Prof. K. Todorova-Hayrabedyan, DSc /