

REVIEW

By: Prof. Radostina Ivaylova Aleksandrova, PhD; Department of Pathology at the Institute of Experimental Morphology, Pathology and Anthropology with a Museum – Bulgarian Academy of Sciences (IEMPAM-BAS); Member of the Scientific Jury according to Order No. NO-05-05-11 of 21.10.2025 of IEMPAM-BAS;

regarding: competition for the academic position of “Professor” in the field of higher education “Natural Sciences, Mathematics and Informatics” in the professional direction 4.3. “Biological Sciences”, scientific specialty “Biochemistry”, for the needs of Department of Pathology at IEMPAM-BAS.

General presentation of the documents in the competition

In the competition announced in the "State Gazette" issue 81 of 03.10.2025 for the academic position of "Professor" at the Department of Pathology of IEMPAM-BAS, only one candidate submitted documents - Assoc. Prof. Dr. Ivan Angelov Iliev from the same Institute. A set of all necessary documents was provided to me in electronic form.

Biographical data for the candidate

Ivan Iliev graduated from the Faculty of Biology of Sofia University "St. Kl. Ohridski" in 2005 as a Master of Science in Molecular Biology - Biochemistry. He briefly worked as a specialist- molecular biologist at the Institute of Molecular Biology - BAS, and in 2006 he joined the Institute of Experimental Pathology and Parasitology - BAS (today IEMPAM-BAS), where he went through all the steps from a third-degree research associate (2006) to the academic position of associate professor, which he occupied after a successful presentation at a competition, in December 2018. In 2012 he acquired the PhD degree in immunology.

Project activity

Assoc. Prof. I. Iliev has participated in the implementation of 13 completed educational (two) or research (11) projects, funded by the Bulgarian National Science Fund of the Ministry of Education and Science and national operational programs. He is currently participating in a project under the National Recovery and Resilience Plan with the base organization University of Chemical Technology and Metallurgy (UCTM), in a COST action and is also a member of the National Center for Biomedical Photonics with the base organization Institute of Electronics – Bulgarian Academy of Sciences.

Teaching / Educational activity

Assoc. Prof. Ivan Iliev has presented a course of 8 hours of lectures in English under the Erasmus program to undergraduate and PhD students from the Department of Medical Biology at Pamukkale University in Turkey. He teaches a course on "Cultivation of Animal Cells" at the Training Center of the Bulgarian Academy of Sciences. Dr Iliev has conducted 4 hours of exercises with undergraduate and PhD students and young scientists on the topic: "Analysis of Biological Effects by Dose-Response Curve". The classes are part of a project funded by the Operational Program "Science and Education for Smart Growth". In the period 2014-2022, he was the supervisor of 7 successfully defended diploma theses for the acquisition of the "Master" degree by students from the UCTM, Department of Biotechnology (4 diploma theses) and Sofia University "St. Kliment Ohridski" - Faculty of Physics (1 diploma thesis) and Faculty of Biology (2 diploma theses).

Publication activity

Dr. I. Iliev is the author / co-author of 119 scientific articles with a total impact factor of 186.541, an individual impact factor of 29.651, which have been cited 415 times (H index = 13). He has 117 participations in national and international scientific conferences. Three of Ivan Iliev's publications are in connection with his PhD thesis (all three have an impact factor, one is in a scientific journal with a quartile Q1, and two - with a quartile Q4). Dr Iliev participated in a competition for the academic position of "associate professor" with 59 publications, 22 of which have an impact factor or impact rank. In the competition for full professor, Ivan Iliev applied with 33 publications with an impact factor, of which 15 in journals with a quartile Q1, 7 with a quartile Q2, 8 with a quartile Q3 and 3 in journals with a

quartile Q4. A list of 257 citations that were not included in the previous competitions for the academic positions of "chief assistant" and "associate professor" is attached.

Expert activity

Assoc. Prof. Ivan Iliev has participated in scientific juries in competitions for the acquisition of PhD degree and for the academic positions of "chief assistant" and "associate professor". He is also a member of the Commission for preparing documents for accreditation of the doctoral program in Biochemistry at IEMPAM.

Compliance of the candidate with the minimum national requirements and additional criteria of the Institute of Microbiology –BAS for occupation of the academic position “Professor”

The analysis of the materials presented by the candidate Assoc. Prof. Dr. Ivan Iliev shows that he covers and significantly exceeds the specified minimum requirements for holding the academic position "Professor" in area 4. Natural Sciences, Mathematics and Informatics, professional field 4.3. Biological Sciences. The data are summarized in Tables 1..

Table 1. Minimum national requirements for occupation of the academic position “Professor”

Group of indicators	Indicators	Required number of points	Ivan Iliev's score based on evidence presented
A	1. PhD thesis	50	50
B	-	-	-
B	Total	100	215
B	4. Habilitation thesis - scientific publications in journals that are refereed and indexed in world-renowned databases of scientific information (Web of Science и Scopus)		215 10 publications: Q1 – 6 publications (6 x 25 = 150 points); Q2 – 1 publication (20 points), Q3 - 3 publications (3 x 15 = 45 points)
Г	Total	220	481
	7. Scientific publications in		456 (23 publications*,

	journals that are refereed and indexed in world-renowned databases of scientific information (Web of Science and Scopus), that are not included in the habilitation thesis		including: 9 in Q1 journals (9x25=225 points), 6 in Q2 (6 x 20 = 120 points), 5 in Q3 (5x15=75 points) and 3 in Q4 journals (3x12=36 points).
	9. An invention, patent or utility model for which a protection document has been issued in accordance with the due process		25 A utility model registered in the Patent Office of the Republic of Bulgaria (Reg. No. 4984 U1)) and
Д	11. Citations in scientific publications, monographs, collective volumes and patents, referenced and indexed in world-renowned databases of scientific information (Web of Science и Scopus)	120	514 A List of 257 citations that were not included in the competitions for the academic positions of Chief Assistant Professor and Associate Professor is presented, 257x2=514
E	Total	150	190
	13. Supervision of a successfully defended PhD student – 50 points.		50 1 successfully defended PhD student
	14. Participation in a national scientific or educational project – 10 points		120 Participation in 12 projects
	15. Participation in an international scientific or educational project		20 Participation in 1 project
Total		660	1450

Main scientific fields and contributions

For participation in the competition for the academic position of "professor", scientific publications published in the period from 2019 to 2025 are included. These publications do not include articles for the ONS "Doctor" and publications used in the competition for the academic position of "Associate Professor".

The articles applied for the competition are published in scientific publications that are referenced and indexed in world-renowned databases of scientific information (Web of Science and Scopus). A total of 33 publications (group of indicators C and D) were applied, of which 26 with an impact factor (total IF: 97.547) and 7 with SJR (SJR: 1.650). The articles are distributed according to the quartile of the journal as follows: in Q1: 15, in Q2: 7, in Q3: 8, in Q4: 3. One utility model is also applied, registered in the Patent Office of the Republic of Bulgaria - registration number 4984 U1, application date: 24.09.2024, validity period: 24.09.2028.

The publications applied in the competition for the academic position of "Professor" reflect the contributions of Assoc. Prof. Ivan Iliev in the following 4 areas:

1. Research on the biological activity of peptide analogues:

Original data on the antiproliferative activity of 17 peptide analogs of BIM-23052 (amino acid sequence d-Phe-Phe-Phe-d-Trp-Lys-Thr-Phe-Thr-NH₂, specifically binds to the somatostatin receptor) with various chemical modifications in human liver cancer (HepG2) and triple-negative breast cancer (MDA-MB-231) cell lines were obtained, as well as information on the relationship between the composition/structure of the analogs and their biological activity.

Three groups of analogs of (KLAKLAK)₂ (consisting of 14 amino acids peptide with antimicrobial and antitumor activity) were studied, in which it was found that the introduction of 1,8 naphthalimide-Gly- and Caf- increases the cytotoxicity and antiproliferative activity of the peptides, but not their selectivity. It has been shown that the length of the peptide chain plays a crucial role in the antiproliferative and antimicrobial activities of the peptide analogues and compounds with promising activity in luminal breast cancer (MCF-7 line) have been identified, along with increased antifungal activity against *C. Albicans* (Si9, Si10). It has been found that the introduction of the unnatural amino acid Nle into the primary structure of (KLAKLAK)₂ – NH₂ does not lead to an increase in antiproliferative activity, but in combination with a second pharmacophore, 1-8-naphthalimide, in the hybrid structure Si17, causes a significant increase in antiproliferative activity. A synergistic effect between the two

parts of the hybrid molecule and the hydrolytic stability of the peptide analogues for 72 hours was observed.

Data on the cytotoxic and analgesic efficacy of FELL peptide analogues were revealed.

For the first time, the photostability of 7 peptide analogues of Aurein 1,2 was reported, among which the Dab-containing analogues exhibited the most stable alpha-helical structure and were recognized as suitable candidates for biological applications.

Data on the structure-activity relationship of temporin A analogues were obtained, for one of the representatives promising antitumor activity in MCF-7 cell line, high selectivity index, low cyto- and phototoxicity, hydrolytic stability was demonstrated.

Original results on the antiproliferative activity of two new aryl hydrazones used in combination with AVPI- and RGD-peptides in MDA-MB-231 cell line were reported.

When studying the biological activity of 17 newly synthesized arylhydrazones derived from nicotinic acid hydrazide and isonicotinic acid, their antiproliferative activity in MCF-7, MDA-MB-231, HeLa, HepG2 and HT-29 cell lines, the lack of phototoxic effect, as well as their low cytotoxicity for MCF-10A and BJ cell lines were established.

New pyrrole-based carbohydrazide and hydrazones were studied for toxicity, phototoxicity and antiproliferative activity in an in vitro melanoma model (SH-4 cell line). The results obtained allowed the synthesis of further modified compounds, among which were found those with significant antiproliferative activity, high selectivity and lack of phototoxic effect, an effect on the cell cycle (accumulation of cells in the S/G2 phase) was established.

Initial data were obtained on the antiproliferative activity of 15 derivatives of 3,5-Diaryl-3,4-dihydro-2H-pyrrole-2-carboxylic Acid in 8 tumor cell lines, with one of them demonstrating high selectivity towards A549 cells (human non-small cell lung cancer).

2. Biological activity of natural products

Original data on the biological behavior of a number of natural products have been obtained, including:

The alkaloid myosmin (3-(1-pyrrolin-2-yl)pyridine), which is found in various widely used foods, has been found to cause a dose-dependent decrease in the survival and proliferative activity of erythroleukemia cells (MEL cell line, clone F4N) and hepatocellular carcinoma (HepG2 cell line). The modulatory effect of vitamin C on the cytotoxic effect of myosmin has been demonstrated. The new knowledge revealed opens the door for further investigation and assessment of the potential health risks associated with the dietary intake of myosmin.

It has been found that some non-volatile compounds obtained from extracts of *Tanacetum vulgare* L. flowers (hydroxycinnamoylquinic acids with 4,5-dicaffeoylquinic acid, flavonoids and their derivatives) have promising antitumor activity in vitro in MCF-7 cell lines.

In studies conducted on bitter apricot kernel extracts, their phytochemical composition, potential for suppressing mutations and recombinations, and their antitumor effect were determined. A high antiproliferative capacity was found in HepG2 (human hepatocellular carcinoma) cells, while non-tumorous human BJ cells were resistant to the action of the extract.

A correlation between antioxidant activity and total polyphenol content in grape marc extracts has been demonstrated, as well as a higher sensitivity of MCF-7 cells compared to MDA-MB-231 cells to their cytotoxic effect.

Information has been revealed on the antiviral activity of essential oil and floral water from *Rosa damascena* Mill against herpes simplex virus type 1 (HSV-1) on rabbit retinal cells.

Data have been obtained on the combined effect of European mistletoe extract (Iscador Qu), applied together with 11 standard, clinically used medicinal products, on MCF-7 and MDA-MB-231 cells.

Experiments with normal and cancer skin cells have demonstrated that encapsulation of the water-soluble form of the essential oil of *Origanum vulgare* ssp. *Hirtum* in micelles with Pluronic F127 and HPC hydrogel reduces the cytotoxic potential of the oil, but preserves its therapeutic potential.

The sensitivity of the MCF-7 and MDA-MB-231 cell lines to the antiproliferative activity of mono- and rhamnolipids (RL-1 and RL-2) has been proven. In MDA-MB-231, a synergistic effect has been registered when combined with cisplatin and RL-2. A mechanism of action of these substances, associated with membrane remodeling through the formation of endosomes, has been proposed.

New knowledge has been revealed about the potential antitumor activity in vitro of 9 hemocyanins and their subunits in cell lines HT-29, 5637, MCF-7, MDA-MB-231 and Graffi tumor. It has been established that it is due to both immune stimulation and a direct effect on tumor cells.

3. Biological studies by differential scanning calorimetry (DSC)

- Differences in the thermodynamic behavior of blood plasma from Wistar rats injected with highly immunogenic egg albumin have been found, with the observed effect being more pronounced in male animals.

- Comparative data on the effects of cisplatin and miltefosine on MCF-10A, MCF-7 and MDA-MB-231 cell lines were obtained, with triple-negative breast cancer cells (MDA-MB-231) showing higher sensitivity than luminal A breast carcinoma (MCF-7).
- Information on the denaturation profiles of blood plasma from patients suffering from early pregnancy loss compared to healthy pregnant and non-pregnant women was reported. The results confirmed the potential of the DSK approach to distinguish pathological changes.

4. Development and testing of new biocompatible coatings

The incorporation of one or more layers of graphene oxide into monolayer structures of hyaluronic acid / chitosan has been found to be among the approaches to regulate the degree of non-specific adhesion of different cell types (human keratinocytes of the HUVEC line and mouse fibroblasts of the BALB/c 3T3 line). These data contribute to revealing new possibilities and approaches for adapting medical devices to cells and tissues.

CONCLUSION

The materials presented by Assoc. Prof. Dr. Ivan Angelov Iliev in connection with the competition show that he fully meets and significantly exceeds the mandatory and specific conditions and scientometric criteria for holding the academic position of "Professor".

With his high professionalism, expert, teaching and organizational skills, he has long earned authority as a respected specialist in the national and international scientific space. The original knowledge and results obtained by Assoc. Prof. Ivan Iliev are a fundamental scientific and scientifically applied contribution in the field of cell biology, biochemistry / pathobiochemistry, molecular and cellular toxicology, medicinal chemistry and biophysics and are a step forward towards overcoming important medical and social challenges of our time, including cancer.

All this gives me reason to confidently propose to the Scientific Jury and the esteemed Scientific Council of IEMPAM-BAS to elect Assoc. Prof. Dr. Ivan Angelov Iliev as PROFESSOR in the professional field 4.3 Biological Sciences (Biochemistry), in the competition announced for the needs of the Pathology department.

17.02.2026 r.

Sofia


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(Prof. Radostina Alexandrova, PhD)