

## REVIEW

**Regarding:** Competition for the academic position of "Professor" at the Institute of Experimental Morphology, Pathology and Anthropology with Museum (IEMPAM) at the Bulgarian Academy of Sciences (BAS) in Professional Field 4.3. Biological Sciences, specialty **Biochemistry**, announced in the State Gazette, issue 81/03.10.2025

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By Order № HO-05-05-11/21.10.2025 of the Director of IEMPAM-BAS, I have been appointed as a member of the scientific jury in a competition for the academic position of Professor at the same institute in the field of higher education 4. Natural Sciences, Mathematics and Informatics, professional field 4.3 Biological Sciences, specialty **Biochemistry**, announced in the State Gazette issue 81/03.10.2025 for the needs of the Pathology Department. One candidate has submitted documents for participation in the announced competition, **Ivan Angelov Iliev, PhD** - Associate Professor in the same institute with scientific and professional experience in the specialty of the announced competition of over 19 years and 7 months. The candidate has submitted all necessary documents required by the Law for the Development of the Academic Staff in the Republic of Bulgaria (LDASRB, amended SG, issue 102 of 23.12.2022), the Regulations for its implementation (amended SG, issue 1 of 6.01.2026) and the relevant regulations of BAS and IMB-BAS, which makes him legitimate to participate in the current competition.

### **Biographical data**

In the period from 1998 to 2005, Assoc. Prof. Iliev acquired Bachelor's and Master's degrees, respectively, in Molecular Biology and **Biochemistry** at the Faculty of Biology of Sofia University St. Kliment Ohridski. In 2011, he defended a doctorate for acquiring a PhD degree in Immunology at IEMPAM-BAS with a dissertation thesis "Study of the immunomodulatory properties of hemocyanins isolated from *Helix lucorum* and *Rapana venosa* in experimental immunotherapy of Graffi myeloid tumor, Guerin ascites tumor and trichinellosis". His career began as a molecular biologist at IMB-BAS, after which from 2006 to 2018 he consistently held academic positions at the Institute of Experimental Pathology and Parasitology at BAS (Research associate 3<sup>th</sup> degree) and at IEMPAM-BAS (Research associate 2<sup>th</sup> degree and Assistant Professor), and from 2018 to the present he has been an Associate Professor in **Biochemistry** in the Pathology Department of IEMPAM-BAS. The scientific activity of Assoc. Prof. Iliev is focused primarily on conducting fundamental and applied research in the field of human and veterinary medicine. *Both the candidate's educational qualification and his entire research activity fully correspond to the specialty of the announced competition in **Biochemistry**.*

### **Scientometric indicators**

The overall scientific output of Assoc. Prof. Iliev to date includes a total of 79 scientific articles, for 15 of which no information was presented. The total IF of the remaining 64 articles is 186.541, and the individual IF of the candidate is 29.651. Articles submitted for participation in the competition do not include articles for acquisition of the PhD degree as well as publications used in previous competitions. All submitted articles are referred to in Web of Science and/or Scopus. The total number of publications for participation in the current

competition is 33 (group of indicators B and G), of which 26 with IF (total IF: 97.547) and 7 with SJR (SJR: 1.650). The articles are distributed according to the quartiles of the journals, as follows: Q1:15, Q2:7, Q3:8, Q4:3. *These data show that in the candidate's assets do dominate articles referred to in Web of Science and those with the highest quartile (Q1).* The candidate's publications include one national patent (utility model) as well. The citations submitted for participation in the competition (group of indicators D) are 257 and do not include citations used in previous competitions (although this is not prohibited by LDASRB and the Regulations for its implementation). The total number of citations of Assoc. Prof. Iliev to date is 415, and his *h*-index is 13, according to Scopus. The candidate also demonstrates a remarkable activity in national and international scientific forums – a total of 126 participations for the entire period of his scientific career. The majority of his participations (87/126), including two plenary lectures by invitation of the organizers, are from the period after Dr. Iliev took the position of Associate Professor.

### ***Review of candidate's publications***

The habilitation thesis (**Group B** publications) of Assoc. Prof. Iliev includes 10 articles, united by a clearly defined and modern scientific topic, namely the study of the biological activity and structure-activity relationship of various classes of peptide analogs with potential antitumor, antimicrobial and analgesic applications. The studies were conducted using modern *in vitro* biological models and well-established cytological and **biochemical** methods. Several scientific topics can be identified within the habilitation thesis. The author carried out the design, synthesis and biological evaluation of **17 new peptide analogs of BIM-23052** (a synthetic analog of somatostatin), aimed at improving the stability, selectivity and antiproliferative activity against tumor cells expressing somatostatin receptors (**B:Nos.1,5,6**). Significant correlations were found between the chemical modifications in the amino acid sequence and the biological effect. A significant result in this aspect represents the observed increase in the antiproliferative activity and selectivity upon introduction of fluorinated phenylalanine residues, as well as the good hydrolytic stability of some analogs. Assoc. Prof. Iliev studied **18 peptide analogs of (KLAKLAK)<sub>2</sub>-NH<sub>2</sub>** (a synthetic peptide with antimicrobial and pro-apoptotic activity), grouped according to their structural features (**B:Nos.3,4,7**). The obtained results convincingly demonstrate that the length of the peptide chain, the inclusion of unnatural amino acids and a second pharmacophore significantly influence both the antiproliferative and antimicrobial activities, as well as the selectivity of the peptides. Peptides with a high selective index and hydrolytic stability were identified, which points to their practical applicability. Assoc. Prof. Iliev also conducted research with a **series of 7 analogs of the FELL-peptide**, which is a bioactive tetrapeptide (Phe-Glu-Leu-Leu), known for its powerful anti-inflammatory and analgesic properties (**B:No.8**). The studies reveal optimal structural combinations for achieving pronounced analgesic activity at significantly lower cytotoxicity compared to the positive controls. The high hydrolytic stability of the analogs reveals their potential for future pharmacological application. Targeted studies were also conducted on **7 peptide analogs of Aurein 1.2** (a peptide with antimicrobial and anticancer properties) with an emphasis on photosafety and antitumor activity (**B:No.9**). Absence of a phototoxic effect and improved antiproliferative activity were demonstrated with some substitutions in the target peptide. Structural analysis by CD-spectroscopy revealed stable  $\alpha$ -helical conformations, directly related to the biological activity of the peptides. The author also performed rational design and synthesis of **4 analogs of Temporin A** (an antimicrobial peptide), one of which demonstrated high

selectivity towards luminal type A breast cancer, low cyto/phototoxicity and excellent hydrolytic stability (**B:No.10**). These results make a significant contribution to the development of peptides combining antimicrobial with antitumor potential. Within the habilitation thesis, the antiproliferative activity of combinations between **2 new aroylhydrazones and AVPI/RGD-peptides** was also evaluated (**B:No.2**). It was shown that despite the high activity of aroylhydrazones alone, their combination with the peptides does not lead to a synergistic effect. The scientific contributions of Assoc. Prof. Iliev, contained in his habilitation thesis, relate to the development of new peptide candidates with potential applications in antitumor therapy, antimicrobial treatment and analgesia, and can be summarized as follows: 1) Demonstration of a structure-functional relationship with several classes of bioactive peptides; 2) Creation and biological characterization of new peptide analogs with high selectivity, stability and low toxicity; 3) Elucidation of the role of unnatural amino acids and secondary pharmacophores in modulating the biological activity.

The presented publications in **Group G** reflect the significant contribution of Assoc. Prof. Iliev in the study of the biological properties of various newly synthesized compounds, natural products and nanomaterials/polymer carriers. Four research areas are outlined in **Group G**: 1) **Study of the biological activity of newly synthesized substances (G:Nos.1,18,21,23)**. In this area, aroylhydrazones, pyrrole-based carbohydrazide/hydrazones and derivatives of 3,5-diaryl-3,4-dihydro-2H-pyrrole-2-carboxylic acid were studied. A relationship was found between the structure and the biological activity of aroylhydrazones, showing that compounds with two hydroxyl and one nitro group exhibit the highest selectivity towards cancer cells. Some pyrrole-based hydrazones demonstrate low cytotoxicity, absence of phototoxic effect and a significant antiproliferative activity, inducing apoptosis and cell cycle arrest. One of the studied derivatives of 3,5-diaryl-3,4-dihydro-2H-pyrrole-2-carboxylic acid demonstrated extremely high selectivity towards lung adenocarcinoma cells; 2) **Study of the biological activity of natural products**. It was found that a) Myosmine (a tobacco alkaloid) shows a dose-dependent reduction in the viability of tumor cells while its combination with vitamin C modulates the cytotoxic effect (**G:No.3**); b) Ethyl acetate extracts from Flores Tanaceti (flowers of *Tanacetum vulgare* (tansy)) show a high antitumor effect and selectivity towards MCF-7 breast cancer cells (**G:No.4**); c) Apricot kernel extract demonstrates a strong antigenotoxic and antirecombinogenic effect, as well as high selectivity and antiproliferative effect towards hepatocellular carcinoma (HepG2) (**G:No.7**); d) Pomace from the Bulgarian grape variety Mavrud has a higher total polyphenol content compared to grape seed extract, and a positive correlation was observed between the antioxidant activity and the total polyphenol content in the extract (**G:No.13**); e) Rose oil products (essential oil and floral water) exhibit a virucidal effect against the herpes virus HSV-1 without inhibiting viral replication (**G:No.22**); f) Combination of European mistletoe extract Iscador Qu with standard chemotherapeutic agents shows a promising synergistic effect in the treatment of breast cancer (**G:No.16**); g) The inclusion of essential oil from *Origanum vulgare* ssp. *hirtum* (Greek/winter oregano) in polymer carriers based on Pluronic F127 micelles and HPC gel reduces the cytotoxicity of the oil, but preserves its potential of a selective and antiproliferative agent against skin cancer (**G:No.19**); h) Two studied rhamnolipids (RL-1 and RL-2) exhibit an antiproliferative effect towards breast cancer and the hypothesis was argued that for achieving a synergistic effect with Cisplatin, most likely RL-2 is needed (**G:No.8**); i) The antitumor activity of 9 hemocyanins, studied *in vitro* and in an *in vivo* model, is due to both direct effects on tumor cells and immune stimulation (**G:Nos.5,6,10,15**); 3) **Biological studies by differential scanning calorimetry (DSC)**. DSC was applied to characterize the effects of

various substances/conditions on cell lines (normal and cancer) (**G:No.9**) and on the proteome of blood plasma from model animals (**G:No.2**) and humans (**G:No.12**). It was shown that DSC can differentiate the thermodynamic profiles of cancer from non-cancer cells, as well as the changes caused by anticancer drugs such as cisplatin and miltefosine. Specific calorimetric markers were identified in the blood plasma of patients with early pregnancy loss, which could be used as a marker for high-risk pregnancy; **4) Creation and testing of new biocompatible coatings.** Biocompatible and biodegradable coatings for medical devices have been developed. It was found that the incorporation of graphene oxide in multilayer structures of hyaluronic acid/chitosan allows precise control over cell adhesion, which is crucial for successful implantation of medical devices (**G:Nos.14,17**). Publications from **Group G** of the candidate also include one methodical (**G:No.11**) and one educational (**G:No.20**) article. Overall, the publications from **Group G** of Assoc. Prof. Iliev demonstrate a wide range of research interests and innovative approaches in **biochemistry** and cell biology, with potential for the development of new therapeutic agents and biomaterials.

### ***Project activity***

Assoc. Prof. Iliev has demonstrated active participation in a number of national and international research projects, covering the period from 2005 to 2027. His project activity is focused mainly on biomedical sciences, with an emphasis on oncology, pharmacology and materials science. The total number of listed projects in which Assoc. Prof. Iliev has participated or is participating is 19, including current and completed ones. Most of the projects are funded by the Bulgarian National Science Fund at the Ministry of Education and Science. The topics include the development of new antitumor and antiviral agents, the study of natural products with antitumor potential, mechanisms of cell death (apoptosis/autophagy), as well as the development of Biophotonics and targeted cancer therapy. The candidate's participation in European and bilateral projects includes projects under EU operational programs (OP HRD) for the development of young scientists, COST Action (INTERCEPTOR) for the study of oral cancer, bilateral cooperation with Russia on the topic of photodynamic therapy, and under the National Recovery and Resilience Plan (BiOrgaMCT). *Overall, the project activity of Assoc. Prof. Iliev is related to a wide range of research topics in the field of contemporary biological sciences and biochemistry.*

### ***Educational activity***

Assoc. Prof. Iliev's educational activity covers lecture courses, practical exercises, as well as successful supervision of MSc and PhD students. Assoc. Prof. Iliev has international teaching experience, including eight lectures in English at Pamukkale University, Turkey. The topics of the lectures are broad and cover modern scientific fields such as: a) Biological properties and therapeutic application of hemocyanins in cancer immunotherapy and therapy of trichinellosis; b) Photodynamic therapy and the application of natural products from *Rosa damascena* and *Rosa alba*; c) Use of differential scanning calorimetry for cancer diagnosis; and d) Antitumor activity of newly synthesized aminophosphonates. In addition, he is teaching the Animal Cell Culture course at BAS with a total of 78 academic hours. He also conducted specialized exercises on the analysis of biological effects by a sigmoidal dose-response curve within a youth project at IEMPAM-BAS.

Assoc. Prof. Iliev's activity as a scientific supervisor and consultant is significant, focused on the training and development of young scientists, mainly at two universities – the University

of Chemical Technology and Metallurgy and the Sofia University St. Kliment Ohridski. Assoc. Prof. Iliev has been a scientific supervisor of five MSc students and a consultant of two in the period from 2014 to 2022. The topics of the diploma theses are interdisciplinary, including photodynamic therapy, nanocomposites, antimicrobial peptides, thermodynamic behavior of tumor cells and anticancer activity of natural products. He has also been a scientific consultant of one successfully defended PhD student in the field of **Biochemistry**. *In conclusion, Assoc. Prof. Iliev's educational activity is versatile, effective and demonstrates his high competence and dedication to the training of young specialists in the field of **Biochemistry** and biomedical sciences.*

### **Compliance with LDASRB**

The following table presents the compliance of the group of indicators from A to E of Assoc. Prof. Iliev with LDASRB, according to Table 1 of the Regulations for ZRASRB implementation (corrected by BAS for indicators G and D):

Indicator group	Minimum points	Candidate's points
A	50	50
B	100	215
G	200 (220 for BAS)	481
D	100 (120 for BAS)	514
E	150	190
<b>Total</b>	<b>640</b>	<b>1 387</b>

*The above table shows that Assoc. Prof. Iliev covers and regarding almost all indicators significantly exceeds the requirements of LDASRB and those of BAS for holding the academic Professor position. His total number of points is more than twice the required minimum.*

### **CONCLUSION**

The analysis made in this review shows that Assoc. Prof. Iliev meets all the formal requirements of LDASRB, the Regulations for its implementation as well as those of BAS and IMB for holding the academic position of a Professor. He meets, and for almost all indicators exceeds, the minimum national requirements for holding this position. His strong points are a clearly defined research profile with an emphasis on the practical implementation of the results. Assoc. Prof. Iliev also demonstrates solid experience in project activity, a responsible attitude towards young scientists and established national and international contacts, which is a solid foundation for his future career development. That is why I confidently recommend to the esteemed Scientific Jury in this competition to propose to the Scientific Council of IEMPAM at BAS to vote **FOR** the election of **Assoc. Prof. Dr. Ivan Angelov Iliev** to the academic position of a **Professor** in Professional field 4.3 Biological Sciences, specialty of **Biochemistry**.

February 3, 2026



Prof. R. Mironova