

REVIEW

by

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on a competition for the Academic position "Professor" at the Institute of Experimental Morphology, Pathology and Anthropology with a Museum, (IEMPAM), BAS; in area 4. Natural Sciences, professional field 4.3. Biological Sciences, scientific specialty "Biochemistry", code 01.06.10, announced in the State Gazette, issue 81 of 03.10.2025, for the needs of the "Pathology" section, IEMPAM, BAS

I. Analysis of the candidate's career profile

The only candidate in the competition, Ivan Angelov Iliev, is a graduate and graduate specialist of the Faculty of Biology of Sofia University "St. Kliment Ohridski" with a Bachelor's degree in Molecular Biology in 2003 and a Master's degree in Biochemistry in 2005. The autobiographical reference shows that his scientific career began in 2003 as a specialist at the Institute of Molecular Biology and later as a fellow at the Institute of Experimental Pathology at the Bulgarian Academy of Sciences. From 2006 to 2018, his career development went through the scientific degrees and titles - research associate III degree with the equivalent of an assistant in the Immunology section at IEMPAM, BAS and research associate I degree with the equivalent of a chief assistant in the Pathology section at IEMPAM BAS. In 2018, Dr. Ivan Iliev held the academic position of "associate professor" in the same section of the institute.

The candidate developed his dissertation on the topic: "Study of immunomodulatory properties of hemocyanins isolated from *Helix lucorum* and *Rapana venosa* in experimental immunotherapy of Graffi's myeloid tumor, Guerin's ascites tumor and trichinosis", and successfully defended it in 2008.

He currently has 19 years of work experience in the specialty.

II. General description of the submitted materials for the competition

The submitted materials for the competition are well arranged and reflect the requirements of the Law and the Regulations for the implementation of the Law on the Development of Academic Staff in the Republic of Bulgaria. The entire history and production of Assoc. Prof. Ivan Iliev is presented, both through an autobiography, lists of publications and citations, and through the presented scientific contributions, and a reference-declaration for fulfilling the minimum national requirements for participation in the competition for "Professor", in area 4. Natural Sciences, Mathematics and Informatics, Professional Direction 4.3. Biological Sciences.

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

The scientometric report shows that Assoc. Prof. Ivan Iliev has 119 scientific articles, of which 64 publications have a total impact factor: 186.541 and an individual impact factor: 29.651. For the purposes of the competition, Assoc. Prof. Ivan Iliev applies with 33 scientific publications, of which 26 publications are in international journals with a total impact factor: 97.547, with his individual impact factor being 13.415. In 29 out of 33 articles he is the lead author, and in 2 publications he is the first author; in 8 of the publications for the competition he is the second author, in 14 articles he is the third author from a multiple team and in 5 publications he is the last author.

Assoc. Prof. Ivan Iliev is a participant in a registered utility model with Reg. No. 4984 U1, Application date: 24.09.2024, Validity period: 24.09.2028, Name: "Anti-caries composition", Owner: KhTMU, Inventors: Dancho Danalev, Irina Uzunova-Raicheva, Iliyan Dobrev, Tsvetelina Foteva, Veronika Nemska, Neli Georgieva, Ani Belcheva Krivirova, Veronika Karadzhova, Kamelia Anichina-Zarkova, Ivan Iliev.

The presented scientific production is very good and has been successfully reflected in the research community through a large number of citations (415 pcs.) and through its presentation in prestigious scientific forums (117 participations). According to Scopus data, Assoc. Prof. Iliev has an h - index of 13.

The candidacy of Assoc. Prof. Ivan Iliev shows that he is also successful in the field of project financing. He has participated in 19 research projects.

Assoc. Prof. Ivan Iliev has teaching experience, expressed in supervision of doctoral students (1 successfully defended doctoral student); supervision of graduates from Sofia University and

the Bulgarian Medical University (7 successfully defended graduates - 5 of them he is a supervisor, 2 he is a consultant). He is the titular of a doctoral course at the Central Scientific Center of the Bulgarian Academy of Sciences, Titular on the topic: "Cultivation of animal cells", 78 teaching hours. The candidate has delivered 8 lectures in English to students and doctoral students at Pamukkale University, Department "Medicinal Biology" - Turkey. 4 hours of exercises were conducted on the topic "Analysis of biological effects, using a sigmoidal dose-response curve. The exercises were conducted with students, doctoral students and young scientists at IEMPAM-BAS, under project BG05M2OP001-2.009-0019-C01.

He has completed 11 specialized courses.

His expert activity is expressed in his participation in scientific juries for the ONS Doctor, Chief Assistant and Associate Professor.

He was a member of the accreditation committee for the specialty "biochemistry".

Description of scientific achievements and thematic areas

Dr. Ivan Iliev's research interests are in several thematic areas, with each area having several areas in which the candidate has contributions:

The candidate develops a coherent and recognizable scientific program between cell biology, biochemistry and biophysics, aimed at experimentally substantiated characterization of bioactive molecules and materials with potential medical applicability. The research is structured around two complementary priorities: (1) discovery and optimization of molecular candidates (peptides, low-molecular synthetic compounds and natural products) with antitumor, antimicrobial, analgesic or antiviral activity and (2) building a reliable methodological framework for assessing efficacy and safety, including mechanistic readouts and biophysical "signatures" of a biological state.

Of the utmost importance is the established experimental infrastructure of cell models and standardized protocols. A cell collection of normal and tumor cell lines has been maintained and developed, new cell lines have been created and characterized, and standardized in vitro tests for cytotoxicity/phototoxicity assessment have been implemented, with the methodology adapted to modern radiation sources (LED-solar simulator). This has direct educational significance through training young researchers in good laboratory practices, standardization of analyses and data interpretation, as well as applied significance through increasing the reliability of preclinical evaluation of candidate materials and compounds.

Profile of scientific activity and thematic directions (2019–2025)

1) Peptide analogs with antitumor, antimicrobial and analgesic activity

The leading thematic core of the candidate is the systematic study of peptide analogs as a platform for creating molecules with improved stability in a biological environment, lower toxicity and increased selectivity towards target cells. In the case of BIM-23052 analogues, it has been shown that specific chemical modifications (including fluorination of Phe) can increase antiproliferative activity and selectivity towards certain tumor lines, and in parallel the hydrolytic stability under different pH conditions has been assessed. In the case of (KLAKLAK)₂ analogues, it has been demonstrated that the chain length, the introduction of a second pharmacophore (e.g. 1,8-naphthalimide) and the inclusion of unnatural amino acids can lead to enhanced antiproliferative and/or antimicrobial effects, with some of the molecules reporting complete hydrolytic stability up to 72 hours and the presence of candidates with pronounced selectivity indices. In separate series (FELL, Aurein 1.2, Temporin A), structural determinants for analgesic and anticancer activity have been deduced and a precise assessment of cyto- and phototoxicity has been made, including the identification of analogues with a favorable activity/safety profile relevant for pharmaceutical applications.

2) Newly synthesized low-molecular-weight compounds: selective antiproliferative activity and mechanistic markers

In the direction of "medicinal chemistry - cellular pharmacology", the candidate evaluates a series of newly synthesized aroylhydrazones and pyrrole-based hydrazones/carbohydrazides, deriving structure-activity relationships and indicating key substituents associated with selectivity towards tumor cells. In addition to standard viability/antiproliferation tests, functional readouts for apoptosis and cell cycle arrest (e.g. accumulation in S or S/G2 phases) are included, which increases the evidentiary value of the results and points towards rational optimization of future molecular series.

3) Natural products and combination regimens: antitumor, antioxidant and antiviral potential

The candidate develops an application-oriented direction for the evaluation of biological effects of natural products and extracts: (i) toxicological-biological effects of nutritional/dietary components (e.g. myosmin and modification of the effect when combined with vitamin C); (ii) phytochemical profiling (LC-HRMS/HPLC-DAD) and functional tests of extracts (e.g. *Tanacetum vulgare*, grape marc from the Bulgarian variety Mavrud) with the establishment of selective antitumor effects and restrictions on non-tumor cells; (iii) antiviral activity of *Rosa damascena* products against HSV-1, with the distinction between an effect on viral particles/adsorption and no significant effect on replication; (iv) search for therapeutic synergies by combining Iscador Qu with standard chemotherapeutics, identifying combinations with a potentially better effect compared to monotherapies, as well as combinations with antagonism, important for clinical caution.

4) Delivery vehicles and formulations: polymer systems and lipid biosurfactants

The candidate contributes to translational solutions for local/controlled delivery by demonstrating the encapsulation of essential oil (e.g. *Origanum vulgare*) in micelles (Pluronic F127) and its inclusion in a hydrogel (HPC) in order to reduce cytotoxicity while maintaining therapeutic potential. Additionally, the antitumor activity of rhamnolipids and their combination with cisplatin was investigated, and under certain conditions a synergistic effect was observed and a membrane-based mechanistic model relevant for the rational design of combination therapies was proposed.

5) Biologically active macromolecules with immunomodulatory potential: hemocyanins *in vitro* and *in vivo*

A significant contribution is made by comprehensive *in vitro*/*in vivo* studies of hemocyanins and subunits in various tumor models, including assessment of lack of systemic toxicity, morphological signs of apoptosis and evidence of antitumor effect *in vivo* (e.g. reduced transplantability, suppressed growth/metastasis, prolonged survival), interpreted as a combination of immune stimulation and direct effects on tumor cells. This direction has a

pronounced applied potential in the field of biomedical biopreparations/adjuvants and experimental oncoimmunology.

6) Differential scanning calorimetry as a biophysical tool for biomarkers and drug effects

The candidate integrates differential scanning calorimetry (DSC) in a biomedical context: (i) characterization of changes in the plasma proteome upon immune stimulation in an experimental model; (ii) comparison of the effects of anticancer agents on non-tumorigenic and tumor cell lines using thermodynamic parameters correlating with treatment sensitivity; (iii) identification of DSC profiles in early pregnancy loss as potential markers for risky pregnancies and their association with inflammatory mediators and genetic polymorphisms. This direction has a clear methodological added value and potential for diagnostic-stratification applications.

7) Biocompatible coatings for medical devices: control of cell adhesion and growth

In the engineering-application direction, the candidate develops multilayer structures (hyaluronic acid/chitosan) with the inclusion of graphene oxide as a means for fine-tuning non-specific cell adhesion and cell growth (including the entire range from prevented to stimulated adhesion) without systemic cytotoxicity. The topic is directly relevant to biofunctionalization of medical devices, where management of cellular response is key to preventing complications and successful integration of implants.

IV. Evaluation of publications submitted for participation in the competition for "Professor"

Scientometric data according to the Law on the Development of Academic Staff in the Republic of Bulgaria were submitted under the procedure, in area 4. Natural sciences, mathematics and informatics Professional field 4.3. Biological sciences, in sub-categories, as follows:

1. By group of indicators "A" - 1. Successfully defended dissertation for awarding the ONS "Doctor" - presented Abstract (50 points out of the required 50 points)
2. By group of indicators "B" - Habilitation work or scientific publications in publications that are referenced and indexed in world-renowned databases - 10 publications were submitted, of which with rank Q1 - 6 pcs; Q2 - 1 pc.; Q3 - 3 pcs. (215 points out of 100 required points)
3. By group of indicators "D" – Scientific publications in publications that are referenced and indexed in world-renowned databases – 23 publications, of which with rank Q1 – 9 pcs.; Q2 – 6 pcs.; Q3 – 5 pcs.; Q4 – 3 pcs.; 1 utility model (481 points out of 220 required points)
4. By group of indicators "E" – Citations in scientific publications, monographs, collective volumes and patents, referenced and indexed in world-renowned databases with scientific information – 257 citations from 38 publications (514 points out of 120 required points)

The required points according to the criteria are significantly exceeded.

V. Conclusion

The candidate presents a mature and consistent scientific output with a clearly recognizable profile: experimentally based design and evaluation of bioactive molecules (peptides, small organic compounds and natural products), combined with methodological competence at the interface between cell biology, biochemistry and biophysics. A strong point is the systematic approach to structure-activity relationships, in which measurable phenotypic effects (antiproliferation, apoptosis, cell cycle, photosafety/cytotoxicity, hydrolytic stability) are used not only for descriptive conclusions, but for the argumentative derivation of principles for the optimization of candidate molecules.

The scientific results are complemented by distinct applied dimensions: promising combinations with chemotherapeutics have been identified, carriers/hydrogels have been proposed to reduce toxicity while maintaining effect, and biocompatible coatings for medical devices with controllable cellular responses have been developed. An important educational and organizational contribution is the construction of a rich cell collection, the creation and characterization of new cell lines and the implementation/adaptation of standardized safety tests (including under conditions corresponding to modern photobiological requirements). These achievements demonstrate the capacity for sustainable development of a scientific school and for the transfer of knowledge and methods in an institutional environment.

The current candidacy fully meets the mandatory and specific conditions and scientometric criteria for occupying the academic position of "Professor".

Assoc. Prof. Ivan Iliev participated in the competition with 33 publications and an abstract, of which 26 publications have an impact factor of 97.547 and 7 issues have an SJR of 1.650. The articles are distributed according to the quartile of the journal, as follows: in Q1: 15 issues, in Q2: 7 issues, in Q3: 8 issues, in Q4: 3 issues. In 88% of the publications, the candidate is the lead author. A utility model registered in the Patent Office of the Republic of Bulgaria has also been applied. The citations applied for the competition are 257 (Scopus) and do not include citations applied in previous competitions.

The scientific works are from the period 2019 to 2025 and are of professional value, with a good publication image, expressed by good citation.

The research of Assoc. Prof. Ivan Iliev has original scientific and applied contributions that have received international recognition. He is a participant in numerous projects, is the supervisor of a successfully defended doctoral student and graduate students.

In conclusion, I confidently vote "FOR" and recommend to the Scientific Jury for this competition to vote on the award of the academic position "Professor" for the needs of the "Pathology" section, IEMPAM, BAS in professional field 4.3. Biological Sciences, scientific specialty "Biochemistry" of Assoc. Prof. Ivan Angelov Iliev, as I believe that he possesses professional qualities that make him suitable for occupying this academic position, which includes scientific research and teaching activities with a tendency to create a school of young scientists, students, graduates and doctoral students, to whom he can pass on the experience accumulated over the years.

14.2.2026

Sofia

Reviewer:



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