

OPINION

By: Prof. Dr. Reneta Toshkova, MD, PhD, IEMPAM-BAS, Member of the Scientific Jury, appointed by Order No. 632/01.08.2025 of the Director of the Institute of Biophysics and Biomedical Engineering – BAS

Regarding the competition for the academic position "Associate Professor" in the field of higher education 4. "Natural sciences, mathematics and informatics", professional direction 4.3. "Biological Sciences", scientific specialty "Biophysics" for the needs of the "Transmembrane Signalling" laboratory of the Institute of Biophysics and Biomedical Engineering (IBPhBME) at the Bulgarian Academy of Sciences (BAS)

Candidate: Assistant Professor Dr. Sonya Nikolova Apostolova, PhD

Materials on the procedure - The only candidate in the competition for the occupation of the academic position "Associate Professor", announced in the State Gazette, issue No.58 of 18.07.2025 is Assistant Professor Dr. Sonya Nikolova Apostolova PhD, from the Laboratory "Transmembrane Signalling" at the Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences (IBPhBME-BAS). The candidate provided all required materials in full compliance with the Law on the Development of the Academic Staff of the Republic of Bulgaria (LDASRB), the Regulations for its Implementation (RILDASRB) and the Regulations on the Conditions and Procedures for the Acquisition of Scientific Degrees and for Holding Academic Positions at IBPhBME-BAS. The electronic documentation is well organised and complete. This opinion has been prepared in accordance with the provisions of the LDASRB, RILDASRB, and the internal regulations of IBPhBME-BAS.

Biographical Data and Career Profile

Assis. Prof. Dr. Sonya Nikolova Apostolova was born in Sofia, Bulgaria. She graduated from the Faculty of Biology at Sofia University "St. Kliment Ohridski" — in 2011 with a Bachelor's degree in "Molecular Biology", and in 2013 with a Master's degree in "Virology". During her studies, she worked as a biologist specialist at the Institute of Experimental Morphology, Pathology, and Anthropology with Museum, Bulgarian Academy of Sciences (IEMPAM-BAS), where she completed her thesis with excellent results. In 2014, Dr. Sonya Apostolova began working as a biologist-specialist at the IBPhBME-BAS. In 2015, she awarded a PhD scholarship at the University of Lleida and the Lleida Biomedical Research Institute (IRB Lleida), Spain. During her doctoral studies, Dr. Apostolova carried out a research internship in the "Cell Signalling and Cell Cycle Control" laboratory at the Faculty of Medicine, University of Barcelona, Spain. In July 2021, she successfully defended her PhD thesis entitled "Role of the NSE1 RING domain in the stability of the Smc5/6 complex and genome integrity in human cells" at the University of Lleida, Spain. Upon returning to Bulgaria, she continued her work at IBPhBME-BAS and, since October 2022, has held the position of Assistant Professor in the Laboratory of "Transmembrane Signalling". Dr. Apostolova has demonstrated strong research activity and project involvement, participating in 8 national and 5 international projects, including one as Principal Investigator under the National Program "Young Scientists and Postdoctoral Researchers" of the Bulgarian Ministry of Education and Science. She has presented her work at 12 national and 6 international scientific conferences, delivering 7 oral presentations and 11 posters. Her scientific achievements have been recognised with numerous scholarships and awards, including two first prizes for Best Poster ("Jubilee Scientific Conference", Sofia, 2022; "International Scientific Conference", Varna, 2024). She is fluent in English, Spanish, and Russian. In 2022, she conducted laboratory exercises in the disciplines "Immunology" and "Tissue Engineering" for fourth-year students at the

University of Chemical Technology and Metallurgy (UCTM) – Sofia, with a total academic load of 60 hours.

These biographical data testify to the dynamic, purposeful, and successful professional development of Dr. Apostolova in the fields of biology, biophysics, genetics, experimental oncology, and regenerative medicine—fully corresponding to the specialization of the announced competition.

Evaluation of Scientific Publications

The total scientific output of Assis. Prof. Dr. Sonya Apostolova includes 21 publications indexed in Scopus and Web of Science, with H-index = 5 (at the submission date) and 84 citations (excluding self-citations).

For the “Associate Professor” competition, Dr. Apostolova presents 15 full-text scientific papers, none of which duplicate works from previous procedures. All articles were published in prestigious, peer-reviewed journals indexed in Scopus and Web of Science, including: *Pharmaceutics*; *International Journal of Molecular Sciences*; *RSC Advances (UK)*; *Biomedicines*; *International Journal of Biological Macromolecules*; *Frontiers in Bioscience – Landmark*; *Clinical Hemorheology and Microcirculation*. Distributed by quartiles are as follows: *Q1* - 8 articles; *Q2* - 4 articles; *Q3* - 3 articles. Thirteen (13) of them are with IF. The total Impact Factor of the presented publications is 40.068. Dr. Apostolova is first author on 3 papers, second author on 3, and third author on 1. She also presents a list of 18 conference participations (12 national, 6 international) and 44 citations (excluding self-citations) in specialized databases (Web of Science & Scopus). Her scientific works, stemming from participation in both national and international projects, demonstrate consistent research activity, scientific maturity, and significant contributions to leading directions in biomedicine.

Evaluation of Contributions

The candidate's contributions include original, confirmatory, and applied results, comprehensively described in her “Author's Report on Scientific Contributions” and can be summarised in three main research directions:

I. Antitumor activity and anti-metastatic potential of novel natural and synthetic molecules in human *in vitro* models. Innovative strategies are proposed for the treatment of various breast cancer types using plant extracts, amino acid ionic liquids, modified proteins, and nanomicelles as selective, effective, and biocompatible agents.

- Standardized *Petasites hybridus* extract shows selective cytotoxic, prooxidant, and apoptotic effects on triple-negative breast cancer cells (MDA-MB231), and antioxidant activity on normal mammary epithelial cells (MCF10-A).

- Six bulgarian *propolis* extracts demonstrate dose- and time-dependent antiproliferative activity—especially those from Gabrovo and Lovech, and this effect is linked with their high phenolic and flavonoid content and compounds such as *chrysin*, *pinobanksin-3-O-propionate*, and *pinocembrin*.

- The modification of *betulinic acid* with amino acid ionic liquids significantly enhances its water solubility and cytotoxicity against hormone-dependent breast cancer cells. The lysine complex [LysOEt][BA] demonstrated the strongest effect (increased cytotoxicity, reduced colony-forming ability, and proapoptotic activity), probably by interaction with estrogen receptors (*ERα*) in cell membranes. The same complexes had a weaker but targeted effect on hormone-independent cells (MDA-MB231), indicating their specificity for that tumor type.

- *Rapana thomasiana hemocyanin*, modified with choline-based and amino acid ionic liquids, exhibits increased antitumor activity and selectivity—strongly inhibiting the proliferation of MCF-7 breast cancer cells while promoting normal fibroblast growth. Hemocyanin complexes with leucine, isoleucine, and tryptophan display considerable cytotoxicity toward MCF-7 cells and no effect on normal fibroblast cells, highlighting their potential as biocompatible antitumor agents.

- *Benzimidazole-hydrazone* incorporated into nanomicelles demonstrates increased cytotoxicity and apoptosis in metastatic breast cancer cells with minimal effects on normal cells, confirming nanomicelles as safe and effective drug carriers.
- A review article summarizes *in vitro* and *in vivo* data on the antitumor activity of alkylphosphocholines and statins, including original findings on erufosine, which induces apoptosis in *Graffi* myeloid tumor cells through cytoskeletal disruption.

II. Biocompatibility of materials for tissue engineering and regenerative medicine

- Hydroxypropyl cellulose hydrogels containing silver nanoparticles exhibit low cytotoxicity, preserved antibacterial activity, and are suitable for 3D wound-healing constructs.
- Complete lack of cytotoxicity and genotoxicity, as well as long-term biocompatibility of hip implant materials, has been demonstrated, making them safe and suitable for clinical use.
- 3D gelatin-based matrices enhance cell adhesion and angiogenesis, as evidenced by increased levels of fibronectin and expression of vascular endothelial growth factor (VEGF) and matrix metalloproteinase (MMP2). Application of a physiological electric field further enhances the effect.

III. Therapeutic approaches for the treatment of diabetic neuropathy and the role of melatonin deficiency in the aging process in *in vivo* models

- The antioxidant *riboflavin* (vitamin B₂) significantly reduces neuropathic pain and improves metabolic balance (increases glutamate/glutamine ratio) in rats with diabetic neuropathy, indicating a novel potential therapeutic effect.
- *Liraglutide* (a drug for the treatment of diabetes) reduces neuropathic pain in mice with diabetic neuropathy through antioxidant and anti-inflammatory mechanisms associated with reduced levels of the inflammatory marker neopterin and an increased glutamate/glutamine ratio.
- In an *in vivo* rat model of aging, melatonin deficiency was found to lead to impaired sphingolipid signalling in the brain in an age-related manner. Elevated levels of ceramide and sphingosine-1-phosphate in the hippocampus of elderly individuals were observed, which is a prerequisite for the development of various neurodegenerative diseases.

The scientific contributions of Assis. Prof. Sonya Apostolova are of high academic value, interdisciplinary nature, and clear applied potential. They reflect profound research work addressing contemporary challenges in experimental oncology, tissue engineering, and biomedicine, demonstrating her capacity to develop innovative concepts, employ modern methodologies, and achieve results of practical importance for medical science and clinical applications.

Evaluation of the Quantitative Criteria

The table below presents the compliance of Dr. Sonya Apostolova's indicators (A–D) with the minimum national requirements, as specified in Appendix 1 of the Regulations for the Implementation of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), adjusted for IBPhBME–BAS by indicators G and D.

Group of indicators	Minimum national +Additional Required Points at IBPhBME	Candidate's Points
A(indicator 1)	50	50
B	-	-
B (sum of indicators 3-4)	100 IBPhBME / LDASRB	100 (5 publications: Q1 – 2; Q2 – 1; Q3 – 2)
Г (sum of indicators 5-10)	220 (IBPhBME)/(200 LDASRB)	225 (10 publications: Q1 – 6; Q2 – 3; Q3 – 1)

Д (sum of indicator 11)	60 (IBPhBME)/(50 LDASRB)	88 (44 citations in indexed journals)
Total number	430	463

The candidate's total score is 463 points (minimum required — 430 points), as detailed in the accompanying table. Dr. Apostolova exceeds the minimum requirements most notably under Indicator D (citations), reflecting her international recognition and scientific impact. Although Indicator E is not mandatory for the *Associate Professor* position, it should be noted that Dr. Apostolova demonstrates substantial project activity. Her extensive experience in the implementation of research projects provides a strong foundation for the successful performance of her future academic responsibilities. The analysis of the scientometric indicators confirms full compliance with the quantitative criteria of the relevant regulations.

CONCLUSION

The analysis of the materials submitted for the competition shows that Assis. Prof. Dr. Sonya Apostolova is a well-established scientist with proven competence in the field of the announced competition. The candidate's scientific production is substantial, characterised by high-quality publications in reputable international journals and a strong citation record. The research findings include original contributions of significant scientific and applied value. The scientometric indicators fully cover the requirements of the LDASRB, the Regulations for its implementation, and the Regulations of the Bulgarian Academy of Sciences and the Institute of Biophysics and Biomedical Engineering for the award of the academic position of "Associate Professor".

All this gives me reason to provide a positive and high evaluation of the candidate's overall scientific activity. I vote "Yes" with conviction and recommend to the esteemed members of the Scientific Jury, as well as to the National Council of the IBPhBME–BAS, the selection of Dr. Sonya Nikolova Apostolova for the academic position of "Associate Professor" in the field of higher education 4. "Natural Sciences, Mathematics and Informatics", professional field 4.3. "Biological Sciences", scientific specialty "Biophysics" for the needs of the laboratory "Transmembrane Signalling" of the Institute of Biophysics and Biomedical Engineering at the Bulgarian Academy of Sciences.

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Sofia

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