OPINION

regarding a competition 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", promulgated in the State Gazette, issue 58/18.7.2025, for the needs of the department "Transmembrane Signaling" at the Institute of Biophysics and Biomedical Engineering (IBPhBME) at the Bulgarian Academy of Sciences

One candidate participated in the announced competition: **Assistant Professor Sonya Nikolova Apostolova, PhD**

The opinion was prepared by: **Assoc. Prof. Tsvetelina Oreshkova, PhD**, member of the scientific jury

The opinion was prepared on the basis of the submitted materials relating to the publication and scientific indicators of the candidate. All necessary documents and scientific works have been attached in a systematic manner and in accordance with the requirements of the regulatory acts of the procedure.

Professional development and qualification

Assistant Professor Dr. Sonya Nikolova Apostolova graduated from the Faculty of Biology at Sofia University "St. Kliment Ohridski" with a "Master" degree in Virology in 2013. She began her research activity in 2011 at the Institute of Experimental Morphology, Pathology and Anthropology with a Museum - Bulgarian Academy of Sciences, where she prepared her diploma thesis. Since December 2014, she has been working as a biologist in the department "Lipid-Protein Interactions" at the Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences. In October 2015, Asst. Prof. Sonia Apostolova enrolled an educational program for obtaining a "PhD" degree at the University of Lleida and the Biomedical Research Institute Lleida, Spain. In 2021, she defended her dissertation on the topic: "The RING domain of Nse1: roles in Smc5/6 complex stability and genome integrity in human cells", and in March 2022 she received the academic equivalent of the degree "doctor" from the Bulgarian Academy of Sciences. In October 2021, she resumed work at IBPhBMI-BAS, and from October 2022 she acquired the academic position of "Assistant Professor". To date, the candidate has accumulated over 5 years and 9 months of work experience in a department of IBPhBME-BAS. During her work activity, she built competencies for the study of migration, invasion, angiogenesis, cytotoxicity, apoptosis and other processes in eukaryotic cells.

Scientific and research activity

Asst. Prof. Apostolova participates in the competition for the academic position of "Associate Professor" with 15 original scientific publications. Thirteen of the publications were published in refereed international and Bulgarian scientific journals with quartiles Q1, Q2 and Q3 (WoS) and a total impact factor of 40.068. Two of the publications are with SJR and quartiles Q1 and Q3 in Scopus. The indicated scientific production was cited by 44 foreign author groups (88 points), which indicates the significance and active interest in the presented topics. The scientific activity is divided into three research areas:

1.) Study of antitumor activity and anti-metastatic potential of new natural and synthetic molecules in human cell models

Asst. Prof. Apostolova is the first author in 3 original publications, outlining a leading thematic direction for studying the potential of various bioactive substances with 1.) **natural origin** (betulinic acid and petasides, isolated from plants (Betula spp, Petasites hybridus); hemocyanins - from Rapana thomasiana and propolis/bee glue) and 2.) **synthetic origin** (erufosine, benzimidazole hydrazone) for specific anti-tumor properties in cell models of breast cancer, etc. In vitro models of human adenocarcinoma metastasis of hormone-dependent (MCF-7) and hormone-independent invasive (MDA-MB-231) cell lines and a non-tumor line (MCF10-A) from mammary epithelium were used. The current studies show different mechanisms of action of anti-proliferative, cytotoxic, pro-oxidative, pro-apoptotic and angiogenic activity of the substances, with increased specificity for tumor lines, but sparing activity for normal cells. The observed differences in the effects are explained by the presence of phenotypic and genotypic differences between cancer and healthy cells, due to the impact on different oncogenic pathways. The established advantage of increased cytotoxicity on tumor cells is a prerequisite for further study and validation of the promising substances for complementary treatment of breast cancer in different hormonal status.

In order to increase the biological activity, solubility and transmembrane transport of some of the substances, the team modified the molecules by adding amino acid residues (obtaining ionic liquids of betulinic acid and hemocyanin) or incorporating benzimidazole hydrazone into micellar carriers.

These studies are innovative, with an important contribution to improving the quality, stability and potential of treatment strategies, as well as to overcoming multidrug resistance.

2.) In vitro study of the biocompatibility of various materials for the purposes of tissue engineering and regenerative medicine

In this topic, Asst. Prof. Apostolova participates in a team that conducts research on the potential of complex-composite hydrogels to create a biocompatible environment to support regenerative processes in tissue damage. Variants of hydrogels with elements of animal (gelatin) or plant (cellulose) origin, or chemical elements with antiseptic properties (silver), have been prepared, which have been studied for biocompatibility and impact on the vitality and functionality of fibroblast, endothelial and tumor cells. The work has reached conclusions indicating biomedical significance, such as 1) maintenance of antiseptic properties of a hydrogel with a silver content below 2%; 2) acceleration of endothelial vascularization in a HUVEC cell model, with significantly increased expression of fibronectin, vascular endothelial growth factor and matrix metalloproteinase 2 in a gelatin hydrogel environment and applied weak direct current (2 V/cm), which contrasts to 3) established suppression

of angiogenic properties and tumor adhesion of a metastatic form of breast cancer under the above conditions.

In another work, validation studies were conducted on the safety of a titanium alloy, widely used in the composition of hip implants in patients.

The section includes 3 articles with 11 citations in Scopus/WoS.

3.) Application of various therapeutic approaches for the treatment of diabetic neuropathy and study of the impact of melatonin deficiency on the aging process in in vivo models

In this area of interest, studies focused on socially significant glucose and melatonin metabolic dysfunctions and the associated conditions of diabetic neuropathy and accelerated aging are presented. Streptozotocin-induced mouse and rat models of diabetes were used to study the antinociceptive properties and the pathways of action of the substances riboflavin and liraglutide on the hyperalgesia response in the observed peripheral neuropathy. Protective activity of riboflavin (vitamin B2) was shown by influencing the immune response and oxidative stress with its participation as a cofactor in the composition of enzymes that neutralize active radicals. On the other hand, liraglutide, which is an incretin mimetic that stimulates insulin release, does not show a direct decrease in blood glucose levels in mice. It alleviates the symptoms of hyperalgesia by controlling the chronic immune response lowering neopterin levels, correcting the glutamine-glutamate ratio in the blood, and in combination with motor and cognitive stimuli in animal husbandry, it shows the best effect.

The role of the antioxidant melatonin in a rat model of aging has been elucidated, in which melatonin deficiency causes sphingolipid dysregulation in the hippocampus of the animals.

Asst. Prof. Apostolova has participated in 13 national and international scientific projects. She has presented her own results at 18 scientific conferences. The current documents convince that she is a qualified, ambitious and promising researcher, with developed skills for teamworking and commitment to the dissemination of scientific results.

Conclusion:

Asst. Prof. Apostolova possesses the scientific indicators of an established scientist with a predominant contribution in the field of tumor biology. Given the quality of her research output, I confirm that she meets the requirements of the Law for the development of the academic staff in the Republic of Bulgaria, the Regulation of the application of the stated Law, and the requirements of the Institute of Biophysics and Biomedical Engineering, and the Bulgarian Academy of Sciences for granting the position of "Associate Professor". Therefore, I suggest to the esteemed Scientific Jury to award Asst. Prof. Sonia Apostolova the academic position of "ASSOCIATE PROFESSOR".

November 24, 2025

Assoc. Prof. Tsvetelina Oreshkova, PhD