ИНСТИТУТ ПО БИОФИЗИКА И
БИОМЕДИЦИНСКО ИНЖЕНЕРСТВО - БАН

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OPINION

in a competition for the academic position "Professor", scientific specialty "Biophysics", professional field 4.3. "Biological Sciences", field of higher education 4. "Natural Sciences, Mathematics and Informatics", announced in SG no. 109 / 21.12.2021 for the needs of the section "Electroinduced and adhesive properties" at IBFBMI-BAS

by Prof. Albena Momchilova, PhD, from IBFBMI, member of the Scientific Jury according to order № 98 / 21.02.2022. of the Director of IBFBMI - BAS.

At the announced competition, the only candidate who submitted documents was Associate Professor Dr. Natalia Alexandrova Krasteva. The materials presented by the candidate are correctly prepared and completed in accordance with the legal requirements.

Brief biographical data about the candidate

Associate Professor Natalia Krasteva graduated from the Faculty of Biology at Sofia University. In 1996 she entered the Institute of Biophysics as a specialist. From 2004 until now she has been working consistently as a research associate and associate professor at IBFBMI-BAS. In 2003 she defended her dissertation on "Interaction of hepatocytes with synthetic membranes - prospects for the creation of an artificial liver"

Analysis of scientific production and scientometric data

The scientific production presented by Assoc. Prof. Krasteva includes 49 publications, 36 of which are in publications with IF. 18 of the publications are in quartile Q1, 5- in Q2, 4 in Q3 and 9 in Q4. 43 participations with reports and posters in national and international scientific forums have been documented. The reference for citations contains 630 titles without auto-citations. According to the data from Scopus, the Hirsch index of Assoc. Prof. Krasteva is 15.

In the competition for the academic position "Professor" Assoc. Prof. Krasteva is presented with 20 publications. The attached reference for scientific production and the achieved scientometric indicators show that the data of the candidate fully cover, and on some of the indicators significantly exceed the minimum requirements for awarding the academic position "professor" set out in the Regulations on the conditions for obtaining scientific degrees and for holding academic positions at BAS. Data for meeting the requirements by indicators are presented, as from group B at required 100 points, 135 points were achieved, from group D at required 220 points 259 points were achieved, from group D at required 120 points - 486 points and from group E at the required 150, 440.82 points have been documented.

Analysis of scientific contributions

Assoc. Prof. Krasteva's research interests are focused in the field of cell biology and the interactions between cells and certain biomaterial surfaces. The contributions from the scientific works presented at the competition can be systematized in the following directions:

- Developments aimed at nanotherapies for use in oncological diseases based on graphene oxide

- Developments related to biological characterization of materials with potential for application in tissue engineering

- Developments related to changes in the organization of chromatin related to cellular aging

A significant part of the publications presented in the competition is aimed at analyzing the biological effects of graphene oxide (GO) and its impact on cancer cells. In this direction, interesting results have been obtained both in purely theoretical and practical terms. A protocol for graphene oxide amination has been developed, which reduces the size of nanoparticles and facilitates their penetration into cells. Concentration-dependent cyto- and mito-toxic effect of graphene oxide was found, as well as lack of genotoxicity of hydroxylamine-aminated graphene oxide. The authors proposed a mechanism of cytotoxicity of aminated graphene oxide, which includes induction of oxidative stress and mitochondrial dysfunction. The established properties of the aminated GO are a prerequisite for its potential participation in complex antitumor therapies.

Some of the studies related to GO are dedicated to PEGylated GO, and the role of PEG is to reduce cytotoxicity to normal tissues and prolong the release time of drugs. PEGylation has been shown to alter the physicochemical properties of graphene oxide and to have a cytostatic effect, increase the DNA-damaging effect of GO and induce apoptosis in certain cancer cells. Tumor suppressor expression has been shown to increase after DNA damage but decreases in HT29 and is not affected by treatment with nanoparticles in Colon26 cells.

The synergistic effect of PEGylated GO in combination with NIR radiation on colorectal cancer cells was also analyzed. A strong synergistic effect of PEGylated GO after laser irradiation in the near IR region with respect to the reduction of the migration capacity of cancer cells has been established. PEGylation combined with NIR irradiation has been shown to have a differential time-dependent and cell-specific effect on DNA damage and cell cycle phases.

Analyzes were also performed on the chemocompatibility of nanoparticles of graphene oxide and PEGylated graphene oxide. PEGylation has been shown to reduce the hemolytic activity of GO and slow the change in erythrocyte morphology. Plasma coagulation studies have shown a positive effect of nanoparticles on plasma fibrinogen levels, which is beneficial for treated patients.

Of interest are the studies on the toxicity of pure and PEGylated GO, as well as polystyrene nanoparticles on nematodes as an in vivo model. The direct target proteins of the main micro-RNAs involved in the signaling pathways of GO toxicity control have been identified. In studying the effect of PEGylated GO on the permeability of the epidermal barrier in nematodes, it was found that the treatment of wild-type nematodes with GO-PEG did not affect the expression of mlt-7 (hem-peroxidase responsible for cuticle replacement), but the treatment of nematodes with a mutation in the mlt-7 gene leads to increased toxicity and translocation of nanoparticles. The research conducted in this direction is useful in elucidating the mechanisms of toxicity of applied nanomaterials, and the information thus obtained could find its application in clinical practice at a later stage.

A significant part of the research work of Assoc. Prof. Krasteva is dedicated to the development and characterization of biomaterials aimed at application in tissue engineering. As more significant

contributions in this area, I would highlight the research on the influence of the method of incorporation of DND particles into silicone polymer in plasma polymerization on the surface properties of composites and the behavior of MCC from rat bone marrow. New data on the effect of substrate elasticity on myogenic differentiation of myoblast cells and murine primary myoblasts isolated from satellite cells have also been published. These studies include the development of hybrid nanofibers with different configurations to promote osteogenic differentiation of mesenchymal stem cells. Studies have shown that the role of fiber arrangement in skeletons is an important factor in stem cell differentiation.

A modern and up-to-date topic developed by the candidate is dedicated to the changes in the organization of chromatin in connection with the aging process. Based on a yeast strain without linker histone, it has been shown that altered chromatin structure with mutation in ARP4 (actin-like protein 4) and without the HHO1 gene for linker histone leads to strong changes in the gene expression profile of a group of genes involved in DNA repair. According to the hypothesis formulated by the authors, the structure of chromatin and the interactions between chromatin proteins are very important factors in maintaining the organization of chromatin in the aging process.

Assoc. Prof. Krasteva was the research supervisor of two doctoral students and three graduates. She has participated in 12 international projects and 11 national projects. She has attended a number of specializations, including the Institute of Chemistry, GKSS Research Center, Teltow, Germany, Pharmaceutical Technology and Biopharmacy, Martin Luther University, Halle, Germany, Institute of Bioengineering in Catalonia, Barcelona, Spain and others.

Conclusion:

Based on all that has been said so far, I believe that Assoc. Prof. Natalia Krasteva is an established specialist with a clearly defined research profile in the field of cell biology and the interaction of cells with biomaterials. Her scientific output is significant in volume and quality and exceeds the requirements for the award of the academic position "professor" set out in the regulations. She has significant experience in leadership and teamwork, competencies and skills for conceptualization and implementation of scientific publications and projects. This gives me reason to strongly recommend that the Scientific Jury vote in favor of awarding the academic position of "professor" in a professional field 4.3. "Biological Sciences", scientific specialty "Biophysics" to Assoc. Prof. Natalia Alexandrova Krasteva.

Sofia, 07/04/2022 Prof. Albena Momchilova, D.Sc.