

## REPORT

on the materials submitted for a competition for the academic position of professor in the field of higher education 4. "Natural Sciences, Mathematics and Informatics", professional field 4.3 "Biological Sciences", scientific specialty "Biophysics", with expertise in modeling cells - biomaterials interactions, for the needs of Department "Electroinduced and Adhesive Properties", Institute of Biophysics and Biomedical Engineering-BAS, announced in SG, no. 109/21.12.2021

by Prof. Dr. Maya Yaneva Velichkova,  
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In the competition for academic positions "professor" for the purposes of section "Electroinduced and Adhesive Properties" announced by the Institute of Biophysics and Biomedical Engineering - BAS (SG, no. 109 / 21.12.2021) participates only one candidate - Assoc. Dr. Natalia Alexandrova Krasteva. All required documents are presented, which meet the requirements of ZRASRB and the Regulations for the terms and conditions for acquiring scientific degrees and holding academic positions in IBFBMI - BAS.

### ***Brief biographical data***

Associate Professor Natalia Krasteva graduated from the Faculty of Biology at Sofia University "St. Kl. Ohridski" with a master's degree in Cellular Biology and Embryology. After graduation she worked as a biologist and in 2001 she began her doctorate at the Institute of Biophysics at the Bulgarian Academy of Sciences (now IBFBMI). In 2003 she successfully defended her doctoral dissertation on "Interaction of hepatocytes with synthetic membranes - prospects for the creation of an artificial liver". In 2010, after a competition, Dr. Krasteva was elected associate professor at the Institute of Biophysics. Dr. Krasteva's scientific activity is related to the main directions of the scientific activity of IBFBMI and is presented in 50 scientific publications, which are reflected in the scientific community with over 240 independent citations.

### ***Scientific metrics***

Assoc. Prof. Krasteva presented a detailed report on the minimum national requirements for holding the academic position of "professor", which correctly reflects her scientific output and shows that these requirements are not only met but also significantly exceeded.

Assoc. Prof. Krasteva has submitted for participation in this competition a list of 21 scientific papers, which include an abstract for the award of educational and scientific degree "Doctor", one chapter in a book and 19 articles in scientific journals. Indicator B includes 7 publications with a total of 135 points, and indicator G includes 12 publications and a book chapter with a total of 259 points. According to both indicators, Assoc. Prof. Krasteva has more than the required number of points according to the requirements of the Regulations for application of ZRASRB in IBFBMI and significantly exceeds the national requirements for the academic position "Professor". Sixteen of all the articles with which Assoc. Prof. Krasteva participates in the competition are in journals with impact factor and three are in journals referred in SJR (with impact rank). It should be noted that most of the publications with IF are in prestigious international scientific journals, and are distributed as follows: 11 are in Q1, 2 are in Q3 and 4 are in Q4. There are six publications in journals with IFs over 5, and in journals with IFs between 3 and 5 there are 5 publications. In most of the materials Assoc.

Prof. Krasteva is a leading or corresponding author, which unequivocally shows her role in the research, proposed hypotheses and analyzes. All publications for participation in the competition are from the period 2018-2021, only one is from 2017, and the chapter of the book is from 2015. The total number of citations of N. Krasteva's publications is 243, as the citations of works, with who have participated in the competition and who are from the last four years already have nearly 80 independent citations. After excluding the self-citations of all authors, Dr. Krasteva's h-index is 13 (Scopus). These scientometric data unequivocally define Dr. Krasteva as an established scientist with active research.

Assoc. Prof. Krasteva is a supervisor of a successfully defended doctoral student. Participated in the development of 7 national and 4 international research projects. She has managed 3 projects at the NSF and 7 international projects at the NSF, DAAD and bilateral inter-academic cooperation. Assoc. Prof. Krasteva has a successful and fruitful collaboration with research teams from Germany, China, Egypt and others, and the results of joint research have been published in prestigious journals. Dr. Krasteva has an active expert activity as a reviewer for international scientific journals, participation in editorial boards, member in scientific juries, which shows recognition of her expertise both in Bulgaria and by the international scientific community.

#### ***Scientific activity and scientific contributions of the candidate***

Over the years, the research activity of Assoc. Prof. Krasteva is dedicated to the study of cell-biomaterial interaction, study of tissue compatibility of synthetic membranes, cell adhesion, protein adsorption, cytotoxicity and chemotoxicity, nanostructured biomimetic surfaces, nanoparticles as drug carriers. The materials presented for review mainly include research in the field of interactions between cells and nano- and biomaterial surfaces, with special attention paid to graphene oxide nanoparticles as particularly promising for use in antitumor therapies.

The presented habilitation report convincingly and arguably presents the relevance and exceptional importance of this topic not only for basic science, but also in terms of application in medicine. The habilitation report on the contribution of the scientific works of Dr. Krasteva is prepared in detail and precisely and correctly reflects the achievements of her research, presented as contributions related to the habilitation work and contributions to publications outside it.

**The contributions from the publications presented as habilitation work** are related to an extensive and in-depth study of the modification of graphene oxide with different functional groups, which changes its physicochemical properties and its reactivity to cancer cells. Here I would like to note:

- The development of a quick and easy protocol for graphene oxide amination with hydroxylamine, which has been shown to reduce the size and negative zeta potential of particles but increase their surface by wrinkling, which properties have a positive effect on particle penetration into cells and opportunities to be loaded with drug (publ. B4);
- Studies on the cyto- and mito-toxicity of hydroxylamine-aminated graphene oxide on hepatocellular cancer cells of the HepG2 line, which show the possibilities for its use in anticancer therapy;
- The established dependences of the cytotoxicity and genotoxicity of graphene oxide aminated with ammonia on the concentration and type of the studied cells are definitely a significant contribution to its application in medicine (publ. B1-B4);
- For the first time, in two types of colorectal cancer cells with different invasive potential, the research of Assoc. Prof. Krasteva show the time dependence of the effect of modification of graphene oxide with polyethylene glycol (PEG) on the expression of several

genes associated with the reparative signaling pathway of ATM of double-stranded DNA breaks.

- A strong synergistic effect of PEGylated graphene oxide activated by near-infrared radiation has been shown in respect of inhibition of the migratory capacity of low-invasive cells (HT29) and the reparative capacity of the studied genes.

**Most of the scientific contributions to the publications combined in indicator G** are related to the development and biological characterization of new materials for application in tissue engineering, such as the development of composite coatings with the ability to control cell adhesion, growth and function and differentiation through changes in the modulus of elasticity of the coating (G7-G13).

- Of interest are the developments on the functionalization of multi-walled carbon nanotubes with amino acids, and the applied for the first time new approach based on sol-technique, which improves their biocompatibility. It has been proven that the created hybrid nanofibers with different configurations and sizes are preferred for osteogenic differentiation of mesenchymal stem cells (G10-G11);

- The scientific findings of *in vivo* studies on the mechanisms of toxicity of graphene oxide nanoparticles using the model system of *C. elegans* nematodes, as well as studies on the chemocompatibility of graphene oxide nanoparticles and PEGylated graphene oxide, are significant contributions to the understanding of the molecular mechanisms of this toxicity (publ. G2-G6);

- The genes involved in the control of graphene oxide toxicity have been identified and two intestinal signaling cascades have been identified that contribute to the effect and localization of graphene oxide nanoparticles;

- Direct target proteins of potentially important micro-RNAs and proteins involved in graphene oxide toxicity control signaling pathways have been identified;

- It has been shown that exposure to PEGylated graphene oxide does not cause toxicity in wild-type nematodes, but is toxic in mutant nematodes deficient in epidermal barrier function, which contributes to understanding the molecular basis for the role of epidermal barrier against toxicity and translocation.

Most of the papers provide new scientific information and new approaches to the biocompatibility of biomaterials, which are a key element in tissue engineering and extremely relevant for their application in medicine. Assoc. Prof. Krasteva's research in the field of biomaterials and especially on the biological effects of graphene oxide and the molecular mechanisms of its toxicity, on the chemocompatibility of graphene oxide nanoparticles and in the field of biological characterization of new materials for application in tissue engineering are original scientific achievements and are significant scientific contributions.

Some intentions for future research have been outlined, which include a new and promising direction related to the study of the factors and molecular mechanisms that mediate premature aging, which will expand and enrich the expertise of Assoc. Prof. Krasteva.

### **Conclusion**

The presented materials convincingly show that Dr. Krasteva is an established scientist working in a topical and significant field of modern science. With her scientific activity Assoc. Prof. Krasteva shows skill for management and development of topics, which is included in the main directions in the scientific strategy of IBFBMI. Most of her research is of an original nature and is a contribution to basic science, but also with significance and exceptional potential for practical application. Dr. Krasteva's national and international contacts show that she is a sought-after partner for scientists from Bulgaria and abroad for

joint research. Dr. Krasteva's scientometric indicators fully cover and exceed both the national and the IBFBMI criteria for holding the academic position of "professor".

I positively evaluate the candidacy of Assoc. Prof. Krasteva to hold the academic position of "professor" and I will vote YES. I recommend to the members of the esteemed Scientific Jury to propose to the members of the Scientific Council of IBFBMI to elect Assoc. Prof. Natalia Krasteva for the academic position "Professor" in the professional field "4.3. "Biological Sciences", scientific specialty "Biophysics".

03. 05. 2022 г .  
Sofia

Signature:  
/Prof. Dr. M. Velitchkova/