

REVIEW

By: Prof. Radostina Ivaylova Alexandrova, PhD, Leader of a work group in Pathology Department, Institute of Experimental Morphology, Pathology and Anthropology with Museum – Bulgarian Academy of Sciences, Part time lecturer in Sofia University “St. Kliment Ohridski”, Faculty of Biology; Lecturer in PhD School of Bulgarian Academy of Sciences; Member of the Scientific Jury by order № 98/21.02.2022 by the Director of the Institute of Biophysics and Biomedical engineering - Bulgarian Academy of Sciences (IBPBME-BAS)

Regarding: competition for the for the occupation of the Academic position “Professor” in Department of "Electro-induced and adhesive properties", Institute of Biophysics and Biomedical engineering Microbiology - BAS, in the field of “Natural Sciences, Mathematics and Informatics”, Professional field 4.3 “Biological sciences”, specialty “Biophysics”.

General presentation of the documents in the competition

In the competition announced in the State Gazette No. 109 of 21.12.2021 for the academic position of "Professor" for the needs of the Department of "Electro-induced and adhesive properties" at IBFBME-BAS, only one candidate submitted documents - Assoc. Prof. Dr. Natalia Alexandrova Krasteva from the same department. The set of all necessary documents precisely prepared by the candidate was provided to me in electronic variant.

Biographical data about the candidate

Natalia Alexandrova Krasteva was born on October 17, 1969. She graduated in Cell Biology and Embryology at the Faculty of Biology at Sofia University "St. Kliment Ohridski" in 1994. In 1996 she started to work as a specialist - biologist in the section "Lipid-protein interactions" of the Institute of Biophysics (Today Institute of Biophysics and Biomedical Engineering) of the Bulgarian Academy of Sciences, where she successively passed the steps of Research Associate II degree (1999-2006), Research Associate I degree (2006-2010) and Associate Professor (since 2010). In the period 2004-2005 she worked as a biologist in the company "Sytonet Sofia - Tissue Bank Ltd." From 2001 to 2003 Natalia Krasteva was a PhD student at IBFBMI-BAS. Her dissertation work, supervised by Assoc. Prof. Dr Georgi Petrov Altankov,

was on the topic: "Interaction of hepatocytes with synthetic membranes - prospects for the development of an artificial liver." After successful defense in 2003, Natalia Krasteva acquired a PhD degree of Biophysics.

Dr. Krasteva has specialized / has been a visiting researcher at the Institute of Chemistry in Teltow, Germany (2 weeks in 1996 and 1997, 1 year in 1999/2000 and 6 weeks in 2000); Cytonet Gmb - a biotechnology company developing products for liver cell therapy in Hanover, Germany (2 months in 2004); Institute for Polymer Research in Teltow, Germany (postdoctoral specialization for 1 year in 2005-2006); Institute of Pharmaceutical Technology and Biopharmacy at Martin Luther University in Halle, Germany (3 weeks in 2007 and 1 month in 2008); Institute of Bioengineering of Catalonia in Barcelona, Spain (1 week in 2009 and 1 month in 2013); University of Ljubljana (2014) and Institute of Zoology, Faculty of Biology, University of Warsaw, Poland (2 months in 2014). Natalia Krasteva is a member of the Union of Scientists in Bulgaria - Section "Biochemistry, Biophysics and Molecular Biology".

From 2015 to 2019 Dr Krasteva was the Head of a section at IBFBMI, she has been a member of the Scientific Council since 2015, and since 2019 she has participated in the Appeals Commission of the Institute.

Dr Krasteva speaks English, Russian and Spanish.

Project activity

Assoc. Prof. Natalia Krasteva is a team – member of 8 national research and educational projects supported by the National Science Fund (NSF) at the Ministry of Education and Science (MES) in Bulgaria (7 projects) and MES - Operational Program "Development of human resources" (1 project) and 9 international research projects funded by the German Research Society (DFG – 2 projects); Roshe Diagnostics, GmbH, Penzberg, Germany; Cytonet Hannover, GmbH, Germany; BMBF-WTZ for cooperation with Bulgaria; agreements for bilateral cooperation between the Bulgarian Academy of Sciences and similar organizations abroad (Romania - 2 projects); European program for cooperation in science and technology (COST) - Actions TD1104 and CA15126.

Associate Professor Krasteva is the Principal investigator of 3 national research projects funded by the NSF and 3 projects supported by DAAD, NSF for bilateral cooperation Bulgaria - China; agreement for bilateral cooperation between BAS and the Egyptian Academy of Research and Technology.

Teaching / Educational activity

The candidate in the competition Assoc. Prof. Natalia Krasteva successfully combines her research activity with training of MSc and PhD students. She is a supervisor of 3 MSc theses and a consultant of 1 MSc thesis of students from Sofia University "St. Kliment Ohridski" and University of Chemistry and Metallurgy. Dr Krasteva is a supervisor of 2 PhD students, one of them successfully defended in 2016, and the other one was enrolled in 2020. Dr Natalia Krasteva was a mentor to 2 undergraduate students (from the Faculty of Biology at Sofia University "St. Kliment Ohridski" and the Faculty of Public Health at Medical University of Sofia) under the program "Student Internships" of the Ministry of Education and Science in Bulgaria.

Publishing activity, patents

The candidate in the competition Assoc. Prof. Natalia Krasteva is the author of 51 publications that have been cited over 650 times (H factor = 15, according to Scopus). Five of the publications are related to her PhD thesis, with 26 (24 articles in scientific journals and 2 book chapters) she participated in the competition for "Associate Professor" and the relevant NACID registration, 20 publications (19 articles in journals and 1 book chapter) have been submitted for participation in the competition for the academic position "Professor". The results of Natalia Krasteva's research activities have been promoted through 43 participations in scientific forums at home and abroad, 3 of the presented posters were awarded.

Expert activity and international cooperation

Proof of the high professionalism of Assoc. Prof. Natalia Krasteva and the authority she has gained in the national and international scientific space is her activity as a reviewer at the National Science Fund of the Ministry of Education and Science in Bulgaria since 2017 as well as in a number of scientific journals (since 2007), referenced and indexed in Scopus, including "International Journal of Artificial Organs", "Progress in Organic Coatings", "ACS applied materials & interfaces", "Acta Biomaterialia, Pharmaceuticals", "Oxidative Medicine and Cellular Longevity", "International Journal Bioautomation". In 2021-2022 she was a guest editor of the journal "Oxidative Medicine and Cellular Longevity".

Assoc. Prof. Krasteva has successful professional cooperation with scientists from academic institutions in Germany, Austria, Italy, Spain, Slovenia, Poland, Egypt and China.

Compliance of the candidate with the minimum national requirements and criteria of the Institute of Biophysics and Biomedical Engineering – BAS for occupation of the academic position “Professor”

The analysis of the materials submitted by the candidate Associate Professor Dr Natalia Krasteva shows that she completely covers the national criteria as well as criteria of the Institute of Biophysics and Biomedical Engineering - BAS for holding the academic position "Professor". The data are summarized in Table 1.

Table 1. Minimum national requirements and criteria of the Institute of Biophysics and Biomedical Engineering - BAS for occupation of the academic position “Professor”

Groups of indicators	Indicators	Required points	Results (Points) achieved by the candidate Natalia Krasteva
A	1.PhD Thesis	50	50
Б	-	-	-
B	Habilitation work - scientific publications in peer reviewed journals indexed in world-famous databases with scientific information (Web of Science and Scopus)	100	137 (7 publications in total: 4 in Q1 journals, 1 in Q3, 1 in Q4 and 1 in journal with SJR)
Г.		220	259
Г7	7. Scientific publications in peer reviewed journals indexed in world-famous databases with scientific information (Web of Science and Scopus).		244 (12 publications in total: 7 in Q1 journals, 1 in Q2, 1 in Q3, 2 in Q4 and 1 in journal with SJR)
Г8	8. Published chapter of a book or		15 1 chapter in a book published by

	collective monograph		Elsevier
Д	11. Citations in scientific publications, monographs, collective volumes and patents, referenced and indexed in world-famous databases with scientific information (Web of Science and Scopus).	120	486 List of 243 citations in journals included in the Web of Science and / or Scopus)
Е		150	440.82
	13. Mentorship to a successfully defended PhD student		50 (1 successfully defended PhD student)
	14. Participation in a national scientific or educational project		70 (Team member in 7 projects)
	15. Participation in an international scientific or educational project		80 (Team member in 4 projects)
	16. Principal investigator of a national scientific or educational project		60 (Principal investigator of 3 projects)
	17. Principal investigator of an international scientific or educational project		150 (Principal investigator of 3 projects)
	18. Raised funds for projects managed by the applicant		30.82 (Total sum 154 400 BGN for 4 projects)

Main scientific directions and contributions

The scientific results and achievements of Assoc. Prof. Natalia Krasteva are in the fields of biophysics, nanomedicine, experimental oncopharmacology, bone tissue engineering and cell aging.

The publications presented in for the competition for occupation of the academic position “Professor” at the Institute of Biophysics and Biomedical Engineering - BAS are 20 in total and reflect the contributions of Natalia Krasteva in 3 main fundamental and scientific-applied areas:

1. Development of nanotherapies for the treatment of cancers based on graphene oxide

New information has been revealed about:

Biological effects of graphene oxide (GO) and its modifications - aminated GO and pegylated GO on cultured tumor cells (from non-small cell lung cancer, colorectal cancer, melanoma), but also in non-tumor cells (human Lep3, canine MDCK). The physicochemical and biophysical properties of these materials are characterized, original data on their cytocompatibility are obtained – regarding their cytotoxic and mitotoxic effect and about their ability to induce DNA damages.

The effect of pegylation of GO on the reparative capacity of cancer cells was studied for the first time by measuring the expression of 5 genes (ATM, RAD51, TP53, BBC3, CDKN1A) involved in the ATM reparative signaling pathway of double-stranded DNA damaging.

The synergistic effect of pegylated graphene oxide in combination with near-infrared (NIR) radiation has been studied. New knowledge has been gained about the dependence of the synergistic effect on cell type (but not on the duration of treatment), about the induction of DNA damage and the influence on the phases of the cell cycle; the lack of effect on mitochondrial function has been established, the influence on the expression of genes involved in the ATM reparative signaling pathway of double-stranded DNA breaks has been proven.

Original results were obtained for the biocompatibility of nanoparticles from GO and pegylated GO.

The mechanisms of toxicity of pure and pegylated nanoparticles from GO and polystyrene nanoparticles in roundworm *Caenorhabditis elegans* (*C. elegans*) have been studied. In the course of the research, the genes involved in the control of the toxicity of GO in the intestine were identified, as well as 2 intestinal signaling cascades (PKC3-SEC8-WTS1 and PKC3-ISP1 / SOD-3) important for activity and localization of nanoparticles.

Direct target proteins of potentially important miRNAs and proteins involved in the signaling pathways responsible for controlling GO toxicity have been identified.

It has been found that the action of *mlt-7* (heme peroxidase responsible for cuticle replacement) in the epidermis is related to the regulation of pegylated GO toxicity and permeability of the epidermis in nematodes.

The profile of miRNA molecules which expression changes in response to pegylated GO is outlined.

A signaling cascade has been found in the insulin cascade pathway, which is activated in the intestines of worms in response to nanopolystyrene particles and regulates their toxicity.

2. Development and biological characterization of materials for application in tissue engineering.

Improved new materials for application in tissue engineering (especially bone tissue engineering) have been developed and biologically characterized - composite coatings with the participation of a detonation nanodiamond with a higher modulus of elasticity; two-layer TiN / TiO₂ coatings deposited on stainless steel; functionalized nanotubes with enhanced antibody-binding ability; hybrid nanofibers of various configurations and sizes to promote osteogenic differentiation of mesenchymal stem cells.

3. Study of the aging -associated changes in chromatin organization

By excluding the corresponding gene, a yeast strain without linker histone was obtained - a convenient model system for studying the mechanisms of chronological aging of cells. The new knowledge gained with this system led to the hypothesis that the structure of chromatin and the interactions between chromatin proteins play an important role in maintaining the organization of chromatin during chronological aging under optimal and stressful (UBA-B) conditions.

Personal impressions from the candidate

We are working with Assoc. Prof. Natalia Krasteva in nearby institutes on similar topics, which became an occasion to meet each other a few years ago. Our very first short professional contact left me with the impression that she is a competent specialist and a responsive and well-meaning colleague. The review of the documents presented in the competition for the academic position "Professor" confirmed to me her image of an erudite scientist with established authority at home and abroad, who persistently and selflessly day after day has accumulated knowledge and skills, worked tirelessly, led by the noble ambition to contribute to solving some of the most important, not only scientific, but also social challenges of our time. It was a real pleasure for me to follow the professional growth of Assoc. Prof. Krasteva and to get acquainted with her contributions and achievements in the rapidly developing fields in which she works.

CONCLUSION

The materials presented by Assoc. Prof. Dr. Natalia Krasteva in connection with the competition show that she fully meets and exceeds the mandatory and specific conditions and scientometric criteria for holding the academic position "Professor". The new knowledge gained by her helps us to clarify the molecular mechanisms determining the toxicity of various nanomaterials (in particular in response to nanoparticles of graphene oxide and its modifications and polystyrene), which will facilitate their application in clinical (oncological) practice; advanced materials have been prepared for bone tissue engineering; original data on the chronological aging of eukaryotic cells under optimal and stressful conditions were obtained.

With her high professionalism, expert, teaching and organizational skills, her ability to team work in the implementation of large-scale and innovative interdisciplinary research projects, her indisputable original contributions in the field of biophysics, nanomedicine, experimental oncopharmacology, bone tissue engineering and cell aging, with her extensive experience in modeling the interactions of biomaterials with cells Assoc. Prof. Natalia Krasteva would be a source of pride for any academic institution. In the challenging times we live, we need scientists like her more than ever, and without a doubt and exaggeration such persons are part of our national wealth.

This gives me reason to convincingly propose to the Scientific Jury and the esteemed Scientific Council of the Institute of Biophysics and Biomedical Engineering at Bulgarian Academy of Sciences to choose Assoc. Prof. Dr. Natalia Alexandrova Krasteva as a PROFESSOR in the Institute of Biophysics and Biomedical Engineering - BAS, in the field of "Natural Sciences, Mathematics and Informatics", professional field 4.3 Biological Sciences (specialty "Biophysics"), for the needs of the Department of "Electro-induced and adhesive properties" at the same institute.

09.05.2022.

Sofia

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