STATEMENT

by Prof. Dr. George Angelov Miloshev,

Head of the Laboratory of Molecular Genetics,
Institute of Molecular Biology "Roumen Tsanev "(IMB) - BAS,
as a member of the scientific jury for the academic position "professor"
a concourse announced by the Institute of Biophysics and Biomedical Engineering (IBFBMI)
– BAS

1. Presentation of the candidate for participation in the concourse, the scientific specialty and the department of the needs of which the concourse is announced.

The concourse for the academic position "professor" in the field of higher education 4 Natural sciences, mathematics and informatics, professional field 4.3, scientific specialty "Biophysics", announced in SG, issue 109 from 21.12.2021.

The concourse was announced for the needs of the section "Electro-induced and adhesive properties".

2. The reason for writing the opinion is my participation in the scientific Jury of the concourse, determined by order № 98 / 21.02.2022 of the Director of the Institute of Biophysics and Biomedical Engineering (IBFBMI).

3. Personal characteristics of the candidate.

Natalia Alexandrova Krasteva holds a Master's degree in Cell Biology and Developmental Biology from the Faculty of Science, Sofia University, Kl. Ohridski "from 1994. She defended her dissertation on" Interaction of hepatocytes with synthetic membranes - prospects for the creation of an artificial liver "and obtained the educational and scientific degree "Doctor " in the scientific specialty 01.06.08 "Biophysics" (Diploma № 14 of October 7, 2323).

From 1996 to the present (25 years) Assoc. Prof. Krasteva works mainly at IBFBMI as a biologist, research associate and associate professor. The interruption of her work in IBFBMI is for 1 year (2004-2005 biologist in "Citonet") and another one year (2005-2006) as a post-doctoral fellow at the Institute of Polymers in Germany.

Assoc. Prof. Krasteva has extensive experience as a researcher in the field of biophysics, especially in the field of cell-biomaterial interactions, cell adhesion, protein adsorption, reorganization of the extracellular matrix and integrin expression in cancer cells, collagen microcarriers for hepatitis transport, tissue compatibility of synthetic membranes, nanoparticles as drug carriers, cytotoxicity, aging.

4. General (quantitative and qualitative) evaluation of research and research activities (based on the submitted documents).

The candidate meets the minimum national requirements under Art. 2b, para. 2 and 3 of ZRASRB in scientific field 4, scientific specialty "Biophysics" and the additional requirements set out in the Regulations for the development of academic staff at the Institute of Biophysics and Biomedical Engineering.

• participation in national research projects: 12; • participation in international research projects: 12; • management of national research projects: 3; • Guide to international research

projects: 3; • Academic experience as an "Associate Professor" at IBFBMI: 12 years; • published scientific publications: 49; • section management: 4 years.

The scientific production of the candidate is completely sufficient in volume and relevant in content of the announced competition.

5. General (quantitative and qualitative) assessment of pedagogical activity.

The candidate meets the minimum national requirements under Art. 2b, para. 2 and 3 of the Law on the Development of Academic Staff at the Institute of Biophysics and Biomedical Engineering.

• management of one successfully defended doctoral student and one doctoral student at the moment (enrolled in 2020); • Guide for graduates: 3 and 1 as a consultant.

6. The contributions from the scientific work of Assoc. Prof. Dr. Natalia Krasteva can be systematized as follows:

• Scientific and applied contributions:

The main research in the scientific papers presented in the concourse is devoted to the interactions between cells and nano- and biomaterial surfaces.

• Contributions related to the development of nanotherapies for the treatment of cancers based on graphene oxide.

The biological effects of graphene oxide and its modifications on cancer cells have been studied. Graphene oxide nanoparticles have been shown to function as effective drug carriers, but also have the potential to exert their own inhibitory effect on tumor cells, and can also serve as photosensitizers. After irradiation with light in the near-infrared region (NIR), they can convert light energy into heat, which can be used in phototherapy of cancer.

The candidate is also focused on the chemical modifications of GO and their importance in the development of therapeutic approaches for various diseases.

• Studies of the biological effect of aminated graphene oxide on cancer cells.

A quick and easy protocol for the amination of graphene oxide with hydroxylamine has been developed. Amination of GO with hydroxylamine has been shown to reduce the size and negative zeta potential of particles, but increase their surface area by wrinkling. Concentration-dependent cyto- and mitotoxic effects of GO nanoparticles and no genotoxic effect of hydroxylamine-amplified graphene oxide (haGO-NH2) particles on HepG2 hepatocellular cells have been demonstrated. Higher and cell-specific toxicity of ammonia-aminated particles of GO was found compared to pure GO in an in vitro study with a set of cell lines. This indicates that the mechanisms of cytotoxicity of pure and ammonia-aminated GO on Colon26 are different in different cell types.

• Studies of the biological effect of PEGylated graphene oxide on cancer cells.

It has been confirmed that PEGylation alters the physicochemical properties of graphene oxide. Increased biocompatibility of GO after PEGylation in melanoma cells and in colorectal cancer cells with different invasive potential, regardless of their invasive potential and the duration of treatment with nanoparticles.

PEGylation has been shown to have a cytostatic effect and enhance the DNA-damaging activity of GO against Colon26 and HT29 cells, depending on the duration of treatment and cell type, but improves the mitochondrial activity of the cells.
For the first time, the effect of PEGylation of GO on the reparative capacity of Colon26 and HT29 cells was studied by measuring the expression of five genes involved in the ATM reparative signaling pathway of double-stranded DNA breaks.
It was found that the expression of the RAD51 gene after treatment with GO-PEG increased many times in Colon26.

• Studies of the synergistic effect of PEGylated graphene oxide in combination with NIR radiation on colorectal cancer cells
A strong synergistic effect of PEGylated GO, activated by laser irradiation in the near infrared region, was observed. PEGylation + NIR irradiation has been shown to have a differential time-dependent and cell-specific effect on DNA damage and cell cycle phases.
For the first time, the synergistic effect of PEGylation of GO and NIR irradiation on the reparative capacity of Colon26 and HT29 cells was studied by measuring the expression of five genes involved in the ATM reparative signaling pathway of double-stranded broken DNA.

7. Citation of the candidate's publications in publications of other authors.
The candidate meets the minimum national requirements under Art. 2b, para. 2 and 3 of ZRASRB in scientific field 4. "Biophysics".
The citations of Assoc. Prof. Krasteva for her participation in the concourse are 243.

8. Admitted weaknesses, critical remarks, recommendations.
I do not have significant critical remarks and recommendations to the candidate.

9. Summary assessment - conclusion and opinion.

Based on the findings of the candidate's research, I propose Assoc. Prof. Dr. Natalia Alexandrova Krasteva for the academic position of "Professor" at the Institute of Biophysics and Biomedical Engineering - BAS in higher education 4. "Natural Sciences, Mathematics and Informatics", Professional field 4.3 Biological sciences, scientific specialty "Biophysics".

Signature:

May 8, 2022

(Prof. Dr. G. Miloshev)