OPINION

regarding the competition for the academic position "associate professor", scientific specialty "Biophysics", professional direction 4.3. "Biological Sciences", field of higher education 4. "Natural Sciences, Mathematics and Informatics", announced in SG no. 32/26.04.2022 for the needs of the "Lipid-protein interactions" section at the IBFBMI-BAS

by prof. Albena Momchilova, member of the scientific jury according to order # 304/30.05.2022of the Director of IBFBMI - BAS.

At the announced competition, the only candidate who submitted documents was Ch. assistant Anelia Kostadinova. The presented materials have been prepared and completed in accordance with the requirements of the regulatory documents.

Brief biographical details of the applicant

Anelia Kostadinova completed her higher education at the Faculty of Biology of Sofia University. During the period 1995-2003 was a biologist specialist at IBF-BAS, from 2003 to 2006 - assistant, and from 2006 Ch. assistant professor at the same institute. In 2012 received a doctorate from the Bulgarian Academy of Sciences in the scientific specialty "Biophysics" on the topic "Modulation of the interaction of cells with polymer surfaces and membranes".

Analysis of scientific production and scientometric data

In connection with the fulfillment of the minimum national requirements for occupying the scientific position "associate professor", Anelia Kostadinova has presented 17 publications and one book chapter, of which 5 are in quartile Q1, 4 - in Q2 and 8 - in Q3. In connection with indicator D11, a list of 32 citations is presented. A list of 15 non-IF articles, which are not referenced in Scopus or Web of Sci and which contain part of the results contained in the reference of contributions, is presented separately. 27 participations with reports and posters in national and international scientific forums are documented. The attached reference for scientific production and scientometric data shows that the candidate's indicators fully cover, and in some of the sections, exceed the minimum requirements for awarding the academic position "associate professor", defined in the Regulations on the terms and conditions for acquisition of scientific degrees and for employment in academic positions. Data are presented for meeting the requirements by indicators, as in group B, with the required 100 points, 105 points were achieved, in group D, with required 220 points, 235 points were achieved, and from group D, with required 60 points, 64 points were achieved.

Analysis of the contributions

Dr. Kostadinova's scientific interests are focused in the field of interactions between cells and certain biomaterial surfaces. The contributions of the scientific works submitted to the competition can be systematized in the following directions:

- Analysis of the interactions of certain types of cells with synthetic and natural materials, as well as with nanoparticles, and the research is aimed at the possibilities of applying the obtained results in the field of biomedicine. The main research approaches on which these studies are based, related to the assessment of biocompatibility and the possibilities of application in clinical practice, are aimed at considering the cytotoxicity and the changes occurring in the cell boundary complex.

- Analysis of the interaction of amphiphilic molecules of natural or synthetic origin with cell membranes. In these developments, along with the fundamental nature of the obtained results, there is also a potential for clinical application at a later stage, especially in the cases of studying anti-tumor agents and the mechanisms by which they interact with membrane components and pass through the cell membrane.

- Developments related to the study of lipid-protein and lipid-lipid interactions, which include the use of model membrane systems with controlled composition and defined functions.

Among the candidate's earlier studies can be attributed the analyzes of the effect of the surface characteristics of materials, such as hydrophilicity, hydrophobicity or roughness, on the structural organization of the cell boundary complex. The results obtained in this aspect serve to evaluate the tissue compatibility of newly synthesized materials and can become the basis for the development of new types of biomaterials with controlled composition and properties.

Research aimed at functionalizing natural or synthetic polymeric biomaterials is of interest. Certain functional requirements for the properties of polymers can be achieved by appropriate polymer surface modification by introducing different functional groups, positively charged, negatively charged and uncharged. In collaboration with a team from HTMU, the author's collective with the participation of the candidate developed synthetic coatings made of polydimethylsiloxane (PDMS), using plasma treatment, followed by grafting acrylic acid with different densities and polyethylene glycol (PEG) with different chain lengths. The authors found that the interaction of cells with modified polyethylene glycol surfaces depends on the length, structure and density of the polymer chains, as well as the presence of COOH groups bound to PDMS. Results of this nature can serve to develop materials with high biocompatibility for the needs of regenerative medicine.

A particularly important direction in the construction of biomaterials with the potential for biomedical applications is the development of functionalized nanoparticles aimed at biomedical applications. The presented publications deal with the creation of metal-containing complexes with improved functional characteristics. The results show that the incorporation of metal compounds into natural polymer structures improves their biocompatibility. Novel collagen/zinc titanate ($ZnTiO_3$) antimicrobial biomaterials have been developed based on sol-gel cryogenic drying technology to preserve the activity of natural collagen. The obtained materials have demonstrated well-expressed antimicrobial activity, moderate cytotoxicity, as well as cell-specific response in in vitro conditions in experiments with human cells of different origin - keratinocytes, fibroblasts and osteoblasts. It has also been shown that chitosan-based nanoparticles are able to influence the ordering and organization of lipids in biomimetic membranes by increasing the degree of ordering of lipid molecules in a concentration-dependent

manner. Four of the presented articles are devoted to improving the properties of graphene with various metals and metal oxides. The results showed that the collagen composite materials with graphene oxide included in them, as well as with added silver or silicon compounds, have antibacterial activity against a wide range of microorganisms and moderate cytotoxicity against human epithelial cells.

Last but not least, the contributions related to the interaction of cell membranes with amphiphilic molecules of natural or synthetic origin should be mentioned. This group of studies includes Bulgarian plants, such as the endemic *Haberlea rhodopensis* and representatives of the *Inula* genus. *Haberlea* extracts were found to affect the actin cytoskeleton of the cells, permeabilize the membrane and disrupt the tight junctions of HaCaT keratinocytes. Myconoside has a similar effect in tests on lung carcinoma cells A549. These studies have been deepened in order to analyze the mechanisms underlying the obtained results. For this purpose, studies were carried out on biomimetic membranes and native cell membranes, and the use of specific fluorescent probes allowed the estimation of the order parameter of lipid molecules in cell membranes. Studies of the action of synthetic antitumor lipids have shown that their combined application with electroporation enhances their cytotoxicity, which is relevant to the administration of lower doses when including them in therapeutic regimens.

Dr. Kostadinova was the scientific supervisor of four graduates at the Department of "Cell Biology and Developmental Biology" at the Faculty of Science at the University of St. Kliment Ohridski" She participated in 20 scientific international and national projects. She has been on several specializations at the Institute of Chemistry, GKSS, Teltov, Germany. She is a member of 3 editorial boards with international participation. From 2004 to 2022, the candidate led exercises and lectures (in 2014) at the Department of "Cell Biology and Developmental Biology" at the Faculty of Science of the University of St. Kliment Ohridski".

Conclusion:

Based on everything presented so far, I believe that Dr. Anelia Kostadinova is a specialist with a pronounced research profile in the field of the interaction of cells with biomaterials. Her scientific output meets the requirements for awarding the academic position of "associate professor", defined in the normative documents. She has significant leadership and teamwork experience. This gives me reason to recommend to the Scientific Jury to vote for awarding the academic position of " associate professor " in professional field 4.3. "Biological Sciences", scientific specialty "Biophysics" to Dr. Anelia Stefanova Kostadinova.

Sofia, 10/08/2022

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