

OPINION

Regarding the competition for the academic position "Associate Professor" in the field of higher education 4. Natural sciences, mathematics and informatics, by scientific field 4.3. Biological sciences, scientific specialty "Biophysics" for the needs of the department "Electroinduced and Adhesive Properties" at IBPhBME - BAS announced in the issue 27/24.03.2023 of State Gazette

By Prof. Antoaneta Vidolova Popova, PhD

Institute of Biophysics and Biomedical Engineering – BAS

Member of the Scientific jury, appointed by the order № 344/19.05.2023 г.
of the Director of IBPhBME – BAS

In the present competition for the academic position "Associate Professor" in the scientific field 4.3. "Biological Sciences", scientific specialty "Biophysics", there is only one applicant, Sen. Assist. Prof. Severina Yordanova Semkova, PhD. In 2011 Severina Semkova received a Bachelor's degree in "Molecular Biology", and in 2013 – a Master's degree in "Biophysics" and completed her post-graduate qualification as a "Teacher of Biology" at the Faculty of Biology of Sofia University "St. Kliment Ohridski". In 2017 she defended a PhD thesis "Combined approach for *in vitro* and *in vivo* visualization of the penetration and localization of fluorescent nanoparticles in tumors cells after electroporation" with scientific supervisors Prof. Romyana Bakalova-Zheleva (Faculty of Medicine of SU), and Assoc. Prof. Bilyana Nikolova (IBBFMI-BAN). In 2016 she joined IBPhBME-BAS as a biologist-specialist, and in 2017 she was elected as a Sen. Assist. Prof. Since 2014 Dr. Semkova has been a part-time lecturer in "Biophysics" at the Faculty of Medicine of the SU, at the Department of "Physics, Biophysics and X-rays" for the specialty "Medicine". Dr. Semkova has published 26 scientific articles (22 in journals with IF, 3 with SJR and one in conference proceedings), which have been cited by independent authors 93 times. The citation rate of scientific works is an indication of the relevance of the conducted research. The total IF of

published articles is 73.371. Dr. Semkova has participated in implementation of 15 research projects funded by Universities, Bulgarian Science Fund and Ministry of Education and 3 international projects. She was the Principle Investigator of 3 projects under the BAS program for supporting young scientists and a beneficiary, coordinator and manager of two projects implemented in Japan. Research results were presented at 34 scientific forums.

Dr. Semkova participates in the current competition for "Assistant Professor" with 17 scientific articles, 15 published in journals with IF and 2 with SJR rank. According to the ranking of scientific journals by quartiles, the published articles are as follows – 4 in Q1 journals, 9 in Q2, 2 in Q3 and 2 in Q4. In 6 of the publications Dr. Semkova is the first author, which is an indication of her substantial contribution. The total IF of the publications included in the competition is 50.23. The H-index after excluding self-citations in SCOPUS is 7. It is noteworthy that 5 of the published articles are in journals with IF above 4.

A completed certificate for the fulfillment of the Minimum National Requirements under Art. 2b of the Law on the Development of the Academic Staff of the Republic of Bulgaria in the field of higher education 4. Natural sciences, mathematics and informatics, scientific field 4.3. Biological sciences, scientific specialty "Biophysics" for the academic position "Associate Professor". According to indicators B, C and D, are presented more than the required points.

An extended reference of the scientific contributions is attached, in which the main achievements are presented, some of which represent new scientific facts.

Dr. Semkova's scientific interests are focused on investigation of cell survival, redox status and other cellular parameters of cancer and healthy cell lines after treatment with conventional and new generation anticancer drugs as well as new natural substances with the aim of improving applied approaches to cancer treatment. Special attention is paid to unravelling the mechanisms of action of various substances that differ by their nature and origin, which is a significant contribution to fundamental research in the field of biology and medicine. A combined treatment with anti-cancer chemotherapeutics and electrical pulses was also applied to achieve an alleviated insertion of the investigated substances into the target cells.

The scientific achievements of Dr. Semkova are presented in two main sections. The **first section** summarizes the contributions, presented in six publications in international refereed scientific journals (Web of Science and Scopus) and grouped in indicator B3 of the Reference list for

the fulfillment of the Minimum National and Specific Requirements – **Habilitation work.** Contributions from *in vitro* studies of the anti-cancer activity of newly synthesized and biologically active substances of natural origin on various breast cancer cell lines are summarized. It was also shown that when combined with electroporation their efficiency was increased. It was shown as well that the mechanism of action of bacterial Trehalose lipid was based on the membrane asymmetry of the lipid bilayer and the formation of endosomes. It was supposed that Trehalose lipid can be potentially applied without possible vascular side effects. Breast cancer cells were affected by application of mono- and di-rhamnolipids which supports the hypothesis that the observed effect was due to autophagy. A synergistic effect was observed when a combined treatment with Rhamnolipids/Cisplatin was performed as a result of remodeling of the cell membrane through the formation of endosomes. By monitoring changes in cell morphology and viability of cancer cells, the anti-cancer effects of conventional anti-cancer drugs, Miltefosine and Cisplatin, which differ in their mode of action, were compared. Significant differences in the thermodynamic profile of cancer cell lines and healthy cells of the same origin (breast cancer) were demonstrated after treatment with the two preparations, which correlates with a change in the conformation of proteins in the cancer cell membrane, matrix and DNA-containing structures. The achievements of the scientific team were presented in a review, summarizing the current aspects and applications of electrochemotherapy, the development and innovations of the application as a complementary method in the modern therapeutic strategies for the treatment of different types of cancer in accordance with the concept of personalized medicine.

The **second section** of the scientific contributions summarizes the scientific significance of the achievements in the published scientific works (11) in refereed and indexed journals (Web of Science and Scopus), grouped in indicator C of the Minimum National Requirements. The **second section** of achievements is divided in 5 subsections.

1. **Development of modern platforms for visualizing the introduction and delivery of substances into cells and tissues in combination/or not with electroporation.** The application of electroporation accelerates the release of organic dyes from chitosan polymersomes with fluorescent contrast substances (quantum dots – QDs), which are a promising model for visualization and prediction of release and targeted delivery of drugs suitable for *in vitro* and *in vivo* applications.

2. Detailed investigation and proving of new aspects of the mechanism of action of conventional anticancer drugs. The regulation and control of cellular redox status during chemotherapy and/or radiotherapy of malignant diseases could find application in the development of new and more effective therapeutic strategies. The administration of conventional chemotherapeutics in combination with Resveratrol or electroporation affects the redox signaling of cancer cells and the induction of oxidative stress, leading to apoptosis and/or necrosis of cancer tissue.

3. Study of the redox status and its relation to cancer treatment. Highly sensitive molecular probes and analytical methods for *in vitro* and *in vivo* mapping of the redox status (Redox Imaging) are being developed to develop new therapeutic approaches in the treatment of significant diseases. An EPR methodology was developed for the registration of superoxide overproduction in living cells and their differentiation (cancer from non-cancer) based on the intracellular redox status. Quantum sensors have been developed for tracking the total reducing capacity and/or oxidative stress in living objects by means of modern visualization techniques (EPR, MRI, optical imaging) based on specificity in their contrast characteristics.

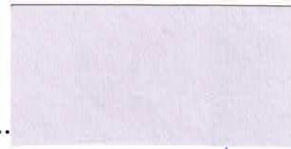
4. Development of modern therapeutic approaches based on changes in redox homeostasis. The redox couples Menadione/Ascorbate and Pro-Vitamin K3/Vitamin C have been shown to have specific efficacy towards the mitochondria of cancer cells based on the generation of a redox imbalance.

5. Identifying and proving new uses of approved and/or tested medicinal products beyond the scope of their original medical indication. Redox-related anticancer activity of an antimalarial drug (Artemisinin) and an antiparasitic drug (Fenbendazole) has been demonstrated, administered alone or in combination with a redox modulator in various cell lines.

In conclusion, I believe that Dr. Severina Semkova participates in the announced competition for the academic position of "Associate Professor" with sufficient volume and quality of scientific works and contributions that exceed the Minimum National Requirements for acquiring the academic position of "Associate Professor" laid down in the Law on Development of the Academic Staff of the Republic of Bulgaria, as well as the specific requirements in the Regulations for its application approved by the Scientific Council of the

IBPhBME for the in the field of higher education 4. Natural sciences, mathematics and informatics, by scientific field 4.3. Biological sciences, scientific specialty "Biophysics". Dr. Semkova's scientific interests and achievements are in the research topic of the Department "Electroinduced and Adhesive Properties" at IBPhBME. I strongly support the selection of Sen. Assist. Prof. Dr. Severina Yordanova Semkova as an "Associate Professor" for the needs of the Department "Electroinduced and Adhesive Properties" at IBFBMI - BAS.

14.08.2023 г.



/Prof. Antoaneta Popova/