



SCIENTIFIC OPINION

by Prof. Dr. Petya Koycheva Hristova

According to the documents of a competition for the academic position "Professor" in the field of higher education 4. Natural sciences, mathematics and informatics, professional area 4.3. Biological sciences, scientific specialty "Cell Biology", announced in the Official Gazette, no. 32 of 09.04.2024

1. General presentation of the procedure:

The competition for a professor in the field of higher education 4. Natural sciences, mathematics and informatics, professional area 4.3. Biological sciences, scientific specialty "Cell Biology" was announced for the needs of the department "Cell Biology and Biology of development", at the Faculty of Biology of SU in SG no. 32 of 04/09/2024. The Scientific Jury was formed by Order No. RD-38-258/05/29/2024 on the basis of Art. 4 and Art. 29a of RSARB, art. 60 of the Regulations for the Implementation of the RSARB and the Regulations for the Terms and Procedures for Acquiring Scientific Degrees and Occupying Academic Positions at SU. The procedure for the disclosure and announcement of the competition provided for in the law and the Regulations has been followed and all the necessary documents have been submitted on time. The competition documentation is well organized and fully reflects the multifaceted educational and research activities of the candidate.

2. Biographical data, career development and professional qualities of the candidate

Only one candidate submitted documents for participation in the competition for the academic position of professor in Professional field 4.3. Biological Sciences, specialty Cell Biology is Associate Professor Dr. **Tanya Ivanova Topuzova-Hristova**.

The candidate graduated from higher education as specialist in "Biology" and a specialization in "Cell Biology and Biology of development" in 1994 at the Faculty of Biology of SU. In 1996, she won a competition for an assistant at the Department of Cytology, Histology and Embryology at the Faculty of Biology and successively held the positions of senior assistant (2000) and chief assistant (2004). In 2008, Tanya Topuzova successfully defended her doctoral dissertation on the topic: "Influence of halogenated inhalation anesthetics on the integrity and reparative abilities of leukocyte cells" and continued her development as a teacher and scientist at the Faculty of Biology. In 2014, she acquired the academic position of "associate professor". Since 2020, she is the head of the Department of "Cell Biology and Developmental Biology" at the Faculty of Biology, and since 2024, she is the deputy dean of the Master's degree of Education.

Therefore, Associate professor Dr. Tanya Topuzova complies with Article 56 of the Regulations on the Terms and Conditions for Holding Academic Positions, as she has held each academic position for a sufficient time, which guarantees mastery of the specific duties and responsibilities listed in the relevant job descriptions.

From the presented resume and scientific works, it is evident a deep interest and accumulated professional experience in various topical problems of cell biology. The professional growth of the candidate is related to the expansion and upgrading of knowledge in the field of the competition through targeted qualifications. Even as an assistant (2000), Dr. Topuzova participated in a six-month specialization in Spain, after which she continued her

development in collaborations with various teams from scientific institutes and universities in the country. The acquired knowledge and experience are essential to establish the candidate as an excellent specialist striving for new aspects of modern cell biology.

On the other hand, Assoc. Prof. Topuzova participated for more than 20 years as a member of the National Olympiad in Biology and Health Education.

3. Evaluation of the candidate's scientific output and scientific metrics

Assoc. prof. Dr. Tanya Topuzova has submitted all the documents necessary for the competition in compliance with the requirements of the RSARB and the Regulations of the SU. They are proposed for evaluation in an overview and systematized with clear distinction.

3.1. General characteristics and evaluation of the scientific publication activity

The scientific output of assoc. prof. Tanya Topuzova is represented by a total of 74 scientific publications, 62 participations in national and international forums and 9 participations in educational aids. It is noteworthy that the publications are mostly in areas affecting various current problems of cell biology, which are strictly in accordance with the theme of the competition.

3.2. Evaluation of citations of scientific works

In the Scopus database, 39 articles in refereed and indexed journals of the applicant are presented, which have been cited (without self-citations) a total of 255 times. Of these, 166 citations are presented for the period 2015-2024. The citation index h factor is 11 (according to Scopus). To participate in the competition for professor, the candidate submits 238 citations, which are from all databases in which published journal articles are referenced and indexed.

3.3. Evaluation of the implementation of the minimum national requirements for the relevant scientific field and the additional requirements of SU "St. Kliment Ohridski"

The minimum national criteria according to the RASRD are fully met by the presented scientometric indicators:

According to **Indicator B**, the requirement of 100 points is fully met by the presentation of 7 publications, of which 2 with Q1, 4 with Q2 and one with Q3, which determine 145 points.

According to **Indicator G**, evidence is presented for 255 points out of the required 200 minimum points, which are formed by 11 articles, of which 8 - Q1, 2 - Q2 and 1 - Q3.

According to **Indicator D**, evidence is presented for 238 citations, which give 476 points and exceed the minimum criterion of 100 points.

According to **Indicator E** In this paragraph, the candidate forms a total of 252 t from participation in projects 170 t, one defended doctoral student - 50 t and attracted funds 32 t with a minimum required 150 t.

3.4. Assessment of teaching and learning activity, scientific supervision of students and administrative and managerial experience

Assoc. prof. Topuzova actively participates in the training of students, graduates and doctoral students. Currently, under her guidance, 14 students have successfully defended their theses. Assoc. prof. Topuzova is the supervisor of 1 doctoral student and 1 full-time student.

The teaching activity of the candidate is related to delivering lectures on Cell Biology for bachelors from BF, on Biology for Special Pharmacy, on General Biology for Special "Teacher of Natural Sciences at the Basic Level of Education", on Control Mechanisms of Cell Proliferation in MP "Cell Biology and Pathology" and "Developmental Biology". She also gives lectures and practical classes on cytology at the Medical Physics Faculty of Medicine, lectures on Cytology and Cell Biology for Biotechnologies, Ecology and Environmental Protection, Biology (correspondence form of education) and others.

The average classroom workload of the candidate for the last three years is 468 hours, and the extra-auditory workload is 731 hours.

3.5. Evaluation of the candidate's project activity

The submitted reference shows the candidate's active participation in national and international projects. Evidence of participation in 15 projects funded by the Scientific Research Institute at the Ministry of Education and Science has been presented, of which Dr. Topuzova is the head of 1 and of which she is the head of a working group. This project activity proves not only the scientific but also the organizational qualities of the candidates.

Conclusion: *The candidate for the current competition for the academic position "Professor", Associate Professor Tania Topuzova-Hristova, meets the minimum criteria of the RASRB and the Rules for its application and exceeds them (1128 total points).*

4. Evaluation of the applicant's original scientific contributions

The research reflected in the 18 scientific works submitted for the competition are in the field of cell biology and can be attributed to two main directions:

- ✓ Biological effects of plant secondary metabolites (potential phytopharmacological preparations) on cultured bacterial and eukaryotic cells;
- ✓ Development of new polymeric nano-sized drug carriers and study of mechanisms of internalization and release of biologically active material in cells.

The contributions of the research work can be systematized as follows:

1. Biological effects of plant secondary metabolites (potential phytopharmacological preparations) on cultured bacterial and eukaryotic cells

A) Phytopharmacological - *in vitro* tests to study the pharmacological potential of Bulgarian medicinal plants

In one part of these studies, the biological effect of a total extract of the endemic resurgent plant silyvrayak (*Haberlea rhodopensis*) and its specific secondary metabolite - phenyl glycoside myconoside - was studied. Total extracts of *Haberlea rhodopensis* increase mitochondrial activity and permeabilize the cell membrane. The sensitivity of proliferating keratinocytes to these extracts allows their use in complex treatment of pathological dermatological conditions, including psoriasis. The potential mechanism of action of purified myconoside has also been studied. Purified myconoside was shown to be able to reorganize membrane lipids by altering the fraction of sphingomyelin-cholesterol-enriched domains.

The contributions of these studies are both fundamental and applied. As a fundamental contribution, I consider the establishment of a direct effect of myconoside on the degree of lipid ordering in the membranes of cancer and non-cancer cells, which leads to a change in their fluidity. Proposing a possible mechanism of action of miconoside explains the observed biological effects. The applied contribution relates to the use of these extracts for the treatment of pathological conditions.

In another part of the research, the potential antitumor activity of extracts of white dead nettle (*Lamium album* L.) on cell cultures was investigated. Extracts from cultivated plants have been found to have better antitumor activity than extracts obtained from natural sources. These results determine the applied contribution for using secondary metabolites as an adjunct to conventional treatments.

Of similar applied contribution are studies on the anti-tumor effect of extracts of white wormwood. The major groups of secondary metabolites identified as chlorogenic (5-CQA), 1,5-, 3,5-, 4,5- and 3,4-dicaffeoylquinic (DCQA) acids, total fraction of flavonoids, flavonoid glycosides, phenolic acids and sesquiterpenes lactones have potential for medical application. Plant species and groups of metabolites with antitumor activity were selected.

The study of the composition and biological effects on normal and tumor cells of rose oil extracts (*Rosa damascene* Mill) also brings significant fundamental and applied contributions. As

a fundamental contribution, I take the phytochemical analysis that reveals the complex composition of rose oil extracts. 14 kaempferol glycosides, 12 quercetin glycosides, 4 phenolic acids and their esters, 4 galloyl glycosides, 7 ellagitannins and quinic acid were identified. The ethyl acetate extract was richer in phenolic and flavonoid compounds and showed better antioxidant activity (DPPH, ABTS and FRAP) compared to the dry extract. An added contribution is the demonstrated low toxicity of both extracts on normal human skin fibroblasts, as well as the significant activity found against *Propionibacterium acnes*, *Staphylococcus aureus* and *S. epidermidis*. These biological activities make the extracts a suitable component for inclusion in cosmetic and medicinal (antibacterial) formulations for skin application. To human hepatocarcinoma (HepG2), the extracts showed a weak antitumor effect until the third day of treatment.

B) *In vitro* tests for the study of biological activity of pharmacological preparations

The main contributions in this part of the research are related to the established role of lipid rafts in sequestering activated ERK1/2 in cells, the internalization of alkylphospholipids through the raft domains of membranes and the differential involvement of the enzymatic and non-enzymatic part of vipoxin (snake venom phospholipase A2) in the displayed cellular response.

2. Development of new polymer nanosized drug carriers and study of the mechanisms of internalization and release of biologically active material in cells.

In this area, new polymer nano- and macro-sized drug carriers have been developed, which have low toxicity, appropriate distribution of the active substance, good internalization and gradual release of the biologically active substance.

The contributions of these studies are applied and fundamental and are related to synthesizing different carriers. The first group are homogeneous coamorphous microsp sponge-type structures with excellent drug loading capacity and controlled desorption profile. Broad-spectrum antimicrobial activity and cell-specific cytotoxicity to model eukaryotic cells were found for the collagen-titanate nanocomposites. Collagen-RGO nanocomposites inhibited the growth of Gram-positive bacteria and *Candida lusitanae*, but were non-toxic to Gram-negative bacteria and human cells. This enables their use as an antimicrobial biomaterial for various biomedical applications, including tissue engineering.

Comb-like polyethylenimines, with different degrees of polymerization, successfully condense linear and plasmid DNA into nanosized polyplex particles, which can be considered suitable systems for gene transfection in eukaryotic cells.

Nanocapsules of pure micelles are suitable for drug delivery and have strong antibacterial activity, while mixed polymer micelles show good antibiofilm and antibacterial activity without membrane disruption or morphological signs of cell death. Conjugates of nucleic acids and polymer have good colloidal stability, increased resistance to nucleases, low cytotoxicity and increased cellular internalization.

In view of the above data, the following conclusion can be made:

CONCLUSION

I highly appreciate the research, teaching and project activities of Associate Professor Dr. Tania Ivanova Topuzova-Hristova. I believe that the candidate fulfills all the requirements of the RSARB and the Regulations for its implementation.

I strongly suggest to the respected scientific jury to evaluate the candidacy of Associate Professor Dr. Tanya Topuzova and to vote positively for the occupation of the scientific position "Professor" in professional area 4.3. Biological Sciences, scientific specialty Cell Biology.

Sofia
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Prepared the opinion:
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