

## **REVIEW**

on the competition

for occupying the academic position of "professor" in a professional direction 4.3. Biological Sciences (Cell Biology), for the needs of the Department of Cell Biology and Developmental Biology", Faculty of Biology, SU "St. Kliment Ohridski", announced in SG no. 32 of 09.04.2024 by Prof. Dr. Rositsa Konakchieva, SU "St. Kl. Ohridski"

### **Normative basis and eligibility of the applicant**

This review was prepared based on order No. RD-38-258 / 29.5.2024 of the Rector of SU "St. Kliment Ohridski" for the appointment of a Scientific Jury for the announced competition for the academic position of "Professor" in 4.3 Biological Sciences (Cell Biology). One candidate appeared in the competition - Tanya Ivanova Topuzova - Hristova, doctor, associate professor, lecturer in the Department of Cell Biology and Developmental Biology, BF of SU "St. Kliment Ohridski". The presented materials are in accordance with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB), the Regulations for the Implementation of ZRASRB, the Regulations for the Terms and Procedures for Acquiring Scientific Degrees and Holding Academic Positions of IBFBMI-BAS. The documentation for the competition is well compiled and comprehensively reflects the candidate's teaching and research activities.

### **Professional Career**

Associate Professor Tanya Topuzova graduated from the Faculty of Biology, SU "St. Kliment Ohridski" as a Master in Biology with a specialization in Cell Biology and Developmental Biology. The dissertation on the topic: "Influence of halogenated inhalation anesthetics on the integrity and reparative abilities of lung cells" was developed under the scientific supervision of Prof. Elena Stefanova and defended at the Department of Cytology BF in 2008. Associate Professor Topuzova has many years of professional experience as a teacher of disciplines in the field of cell biology. Since joining the Department of Cytology, Histology and Embryology, she has been fully involved in teaching activities: she started at BF in 1996 and until 2004 was successively an assistant and senior assistant leading practical classes in Cytology, Cell Biology (basic courses); Cell Cultivation and Cell Nucleus (specialized courses); Animal cell cultures and hybridoma techniques

- basic training courses in the Bachelor's degree and Cell Cultivation (module culturing animal cells) - course in MP in Cell Biology and Pathology and Developmental Biology, actively participates in conducting scientific research, etc. From 2004 to 2014 he held the position of chief assistant and lectured in Cytology and Cell Biology for bachelors, majors in Biotechnology, Ecology and Environmental Protection and Biology in part-time study; lectures on Cytology, Histology and Embryology (Cytology module) for bachelors, major Biology and English Language Teachers; lectures on Control mechanisms of cell proliferation in MP on Cell Biology and Pathology and Developmental Biology; Lectures and practical classes in Cytology at the Faculty of Medical Physics. As an associate professor, Tanya Topuzova has been leading since 2014 LECTURES ON CELL BIOLOGY FOR UNDERGRADUATES, SPECIALTY BIOLOGY; BIOLOGY LECTURES FOR SPECIAL. PHARMACY; GENERAL BIOLOGY LECTURES FOR SPEC. PRIMARY LEVEL SCIENCE TEACHER; LECTURES ON CONTROL MECHANISMS OF CELL PROLIFERATION IN MP IN CELL BIOLOGY AND PATHOLOGY AND DEVELOPMENTAL BIOLOGY; LECTURES AND PRACTICAL LESSONS ON CYTOLOGY IN THE SCHOOL OF MEDICAL PHYSICS.

Associate Professor Topuzova has been a member of the National Commission for the Olympiad in Biology and Health Education for over 20 years. Participation in scientific projects is mainly expressed in leadership and/or in work groups for the implementation of specific tasks under scientific contracts - a total of 21, 6 of which were presented them financed by SU "St. Kliment Ohridski". He is the head of two projects from 2003 and 2009 at the FNI of MOMN with topics in the field of cell signaling in in-vitro and 3D-in-vivo models, participates in teams of a number of other projects with a wide thematic scope in areas such as bio- and nanotechnologies, microbiology, plant physiology, etc. in his capacity as an expert in cell biology and model in-vitro systems for the purposes of toxicological analysis. As a result of successful cooperation with teams from BAS institutes, in particular Inst of Polymers, Inst of Organic Chemistry, IBFBMI, etc., Dr. Topuzova had the opportunity to participate in multidisciplinary teams, as a result of which publications were published scientific articles with an impact factor and high citation index.

Associate Professor Topuzova was the scientific supervisor of a PhD student in 4.3., Cell Biology, in the period 2002-2022 she supervised 14 graduate students (masters and bachelors) in the MP Cell Biology and Pathology. He has extensive experience as a mentor in the Student Practice program of the Ministry of Education and Culture.

## **Scientific contributions of the candidate**

Dr. Topuzova's scientific research activity corresponds to the scientific specialization of the competition - cell biology, with a focus on membrane physiology, cell behavior and vitality, adhesion properties and cell-cell, cell-host interactions, etc. The presented general list of scientific publications presents 63 scientific papers (including 7 articles in full text in the Yearbook of SU "St. Kliment Ohridski" which could be referred to articles in a collection - 9 in number according to the presented list), as well as one teaching aid (to the list of teaching aids where 15 are cited). In a separate list "Participations in conferences" 67 sectional reports and posters are cited without specifying the event at which they were presented, with the exception of one poster published in the FEBS Journal - the list thus presented is incomplete and beyond the scope of the review.

In the scientific reference platform SCOPUS at link <https://orcid.org/0000-0002-1575-0790> the total number of scientific publications of the candidate is 39, cited 257 times, h-index 10; in other databases (Google Scholar) respectively 61, cited 444 times, h-index 13.

In the competition for "professor" Prof. Topuzova participated with 7 scientific publications in publications that are referenced and indexed in world-famous databases with scientific information (Web of Science and Scopus), as well as 5 more articles in non-refereed journals on the subject of weight of habilitation work under item 4. The total IF of the refereed articles is 24.7, the individual one – 2.92 with an average number of co-authors of 10. In two of the publications, Dr. Topuzova is the third author, in tother two – the last. This brief analysis and taking into account the professional experience of Assoc. Topuzova allows to outline scientific contributions in two main directions:

1. Design of in-vitro bacterial and eukaryotic cell models for testing biological effects of plant secondary metabolites (potential phytopharmacological preparations)

- Phytopharmacological - in vitro tests to study the pharmacological potential of Bulgarian medicinal plants. Research contributions relate to a direct effect of myconosides on the degree of lipid ordering in the membranes of cancer and non-cancer cells, which affects their vitality, organization of the actin cytoskeleton and proliferative activity. The change in fluidity has also been confirmed in biomimetic membranes. (publications 01, 04, 05, 07).
- Main groups of secondary metabolites from a total of nine species of plants found in Bulgaria (*Inula oculus-christi* L., *I. bifrons* L., *I. aschersoniana* Janka var. *aschersoniana*, *I. ensifolia* L., *I. conyza* (Griess .) DC., *I. germanica* L., *I. helenium*, *I. salicifolia*, *I. spirelifolia*) with medicinal

potential, with a focus on chlorogenic (5-CQA), 1,5-, 3,5-, 4,5- and 3,4-dicaffeoylquinic (DCQA) acids, total fraction of flavonoids, flavonoid glycosides, phenolic acids and sesquiterpene lactones. When studying critical concentrations of cytotoxicity and in vitro biological activity in various cancer and non-cancer cell lines, plant species and groups of metabolites with potential for antitumor action were determined (publications 02, 06, 09, 10).

- The detailed phytochemical analysis of two rose oil extracts (*Rosa damascene* Mill.) on normal and tumor human cells was investigated, including 14 kaempferol glycosides, 12 quercetin glycosides, 4 phenolic acids and their esters, 4 galloyl glycosides, 7 ellagitannins and quinic acid. The ethyl acetate extract was found to be richer in total phenolic and total flavonoid compounds and showed better antioxidant activity (DPPH, ABTS and FRAP) than the total dry extract, low toxicity for both extracts on normal human skin fibroblasts, as well as significant activity against *Propionibacterium acnes*, *Staphylococcus aureus* and *S. Epidermidis*. The developments have an applied nature, presenting a full characterization of potential candidates for inclusion in cosmetic and medicinal (antibacterial) formulas for skin application. (post 03)

- A role for lipid rafts has been established in sequestering activated ERK1/2 in cells grown in 3D conditions similar to in vivo, to reduce their level of proliferation; internalization of alkylphospholipids through the raft domains of membranes, leading to the influence of lipid-dependent signaling pathways in a cell-specific manner and different involvement of the enzymatic and non-enzymatic part of vipoxin (phospholipase A2 from snake venom) in the manifested cellular response - induction of cellular death or high genotoxicity. (posts 18, 20, 22, 23)

2. Research on mechanisms of internalization and release of biologically active material in cells when testing new polymer nanosized drug carriers:

I accept the following contributions from this body of research that can be referred to this competition:

- Broad-spectrum antimicrobial activity was found for the collagen-titanate nanocomposites, as well as cell-specific cytotoxicity for model eukaryotic cells (osteosarcoma, fibroblast and keratinocyte cells), both depending on the concentration of ZnTiO<sub>3</sub>. Collagen-RGO nanocomposites are active toward Gram-positive microorganisms and *Candida lusitanae*, but

nontoxic toward Gram-negative and human cells, making them a promising antimicrobial biomaterial for various biomedical applications, including tissue engineering;

- In human cells, the internalization pathways and transfection efficiency of polyplex nanoparticles depend on the topology of the polymer chain. Vector systems based on polymers with a denser structure can be considered promising systems for gene transfection in eukaryotic cells;
- Extremely low cytotoxicity and insignificant damage to the cell membranes of human cells of nanocapsules of amphiphilic triblock copolymer cationic micelles with DNA was found, which makes them suitable for carrying medicinal preparations. Clear micelles loosen the bacterial biofilm matrix and cause changes in the bacterial surface. Micelles loaded with AgNO<sub>3</sub> successfully destroy bacterial biofilms and have a strong antibacterial effect;
- Mixed polymeric micelles of cationic and nonionic copolymers in different ratios, alone or loaded with the antibiotic ciprofloxacin showed good antibiofilm and antibacterial activity and composition-dependent cell viability in human cells without membrane disruption or morphological signs of cell death;
- Conjugates of nucleic acids and polymer (a new class of polymeric nanoparticles called spherical nucleic acids) have good colloidal stability, increased resistance to nucleases, low cytotoxicity and increased cellular internalization.

(posts 02, 13, 14, 15, 16, 17, 19, 21, 24)

#### **Assessment of compliance with mandatory minimum requirements**

In summary, the presented scientometric indicators according to ZRASRB and PPZRASRB, by area 4. Natural sciences, mathematics and informatics Professional direction 4.3. Biological Sciences, in sub-categories, are as follows:

1. According to group of indicators "A" - 1. Successfully defended dissertation for the award of ONS "Doctor" - 50t.
2. By group of indicators "B.4" - Habilitation work or scientific publications in publications that are referenced and indexed in world-famous databases with scientific information (Web of Science and Scopus). 7 publications with a total impact factor of 24.7 are presented, of which with rank Q1 – 1 publication; Q2 – 5 pcs.; Q3 – 1 pc. (140 items out of required 100 items). In two of them,

the candidate is the third author, in the other two - the last, which testifies to her contribution to the development of the relevant problem.

3. According to group of indicators "D" - Scientific publications outside the habilitation work in publications that are referenced and indexed in world-famous databases, 11 referenced and indexed publications, as well as two other non-referenced articles and 9 study aids are presented. The overall impact factor for these publications is 34.58 and they are distributed by quartiles as follows: rank Q1 –8 items; Q2 – 2 pcs., Q3-1pc. (255 out of required 220t.)

4. By group of indicators "D" - Citations in scientific publications, monographs, collective volumes and patents, referenced and indexed in world-famous databases with scientific information - in SCOPUS without self-citations - 166 items. (332 items)

I accept as fulfilled the minimum national requirements under Art. 2b of ZRASRB, as well as those of SU "St. Kliment Ohridski" for professional direction 4.3 Biological Sciences.

**In conclusion,**

This application is in accordance with the minimum national requirements for occupying the academic position "professor", as well as with the specific requirements specified in the Regulations for the implementation of the law on the development of the academic staff in the Republic of Bulgaria at SU "St. Kliment Ohridski". Given the overall professional teaching and research activity of Associate Professor Tanya Topuzova Hristova, which outlines a significant volume of teaching and teaching activity and quality scientific production, I strongly recommend to the Honorable members of the Scientific Jury appointed by Order No. RD-38-258 / 29.5.2024 of the Rector of SU "St. Kliment Ohridski" to propose to the Faculty Council of the Faculty of Biology that Associate Professor Dr. Tania Ivanova Topuzova - Hristova be elected to the academic position of "Professor" in Professional Direction 4.3. Biological Sciences (Cell Biology).

29.07.2024

Signature:

/Prof. Rositsa Konakchieva, DSci/