

STANDPOINT

Considering the competition for the academic position "Professor" in the area of higher education 4. Natural sciences, mathematics and informatics, professional field 4.3. Biological Sciences, scientific specialty "Biophysics", announced in the State gazette issue 94 dated November 12, 2021

for the needs of the department "Biomacromolecules and biomolecular interactions", Institute of biophysics and biomedical engineering, Bulgarian Academy of Sciences

by Prof. DSc Stefka Germanova Taneva, Institute of biophysics and biomedical engineering, Bulgarian Academy of Sciences

The only candidate in the competition is Assoc. Prof. Dr. Svetla Jeliaskova Todinova.

Dr. Todinova is an electronics engineer, graduated from the Technical University, Sofia, in 1982. In 2013 she defended her dissertation on "Thermodynamic profile of plasma proteome in malignant diseases" and obtained the scientific and educational degree "Doctor".

She began her scientific career as a constructor at the Institute of Electronics - BAS, from 1986 to 1988 she was a research associate (now assistant) at the NPP "Pulma" - BAS. In 1988 she started working at the Institute of Biophysics - BAS as a senior assistant, and in 2018 she acquired the academic position "Associate Professor" in the department of "Biomacromolecules and Biomolecular Interactions", Institute of Biophysics and Biomedical Engineering – BAS, where she currently works.

Scientometric data Assoc. Prof. Dr. Todinova has 57 publications, 54 of which have an impact factor. 395 citations (WEB of Sci) were noted, h-index 12 (Scopus).

Assoc. Prof. Todinova participated in the competition with a total of 26 articles published after her habilitation as an Assoc. Prof., 25 of them with an impact rank (Q1 - 7 articles; Q2 - 11 articles; Q3 - 7 articles); 25 with impact rank (24 with an impact factor and 1 with SJR), and 1 without impact factor / rank. She is the first author of 7 and corresponding author of 6 of the publications. 9 of the publications are included in a habilitation work on "Temperature and conformational stability of native proteins in biological samples and model systems. Application in biomedicine".

According to the presented report, the total number of points on the indicators for the national requirements for holding the academic position "professor" is 1136 points (A (50), B (170), D (335), E (342) and E (239)), almost twice as higher as the minimum national requirements (600 points) for holding the academic position "professor".

Assoc. Prof. Todinova has been actively involved in the research work of the Department of Biomacromolecules and Biomolecular Interactions established in 2010, in the development of research projects and guidance of young scientists, and has extensive experience in various aspects of differential scanning calorimetry.

Associate Professor Todinova is coordinator of 1 project at NSF and has participated in the research teams of 19 research projects (2 projects at NSF, 1 COST project, 4 projects with the Medical University - Pleven, 2 youth projects and 6 EBR projects).

Assoc. Prof. Todinova was co-supervisor of a successfully defended doctoral student and supervisor of a full-time doctoral student.

She has conducted laboratory exercises in differential scanning calorimetry for students from the Faculty of Biology at Sofia University and students in the Operational Program "Human Resources Development".

Scientific contributions

The habilitation work includes studies of denaturation of the major proteins in blood serum from patients with multiple myeloma (MM) and Waldenström's macroglobulinemia (publications 1, 2) and in blood plasma from experimental models with induced pre- and neoplastic lesions in the colon and inflammation (publications 3,4); of membrane and cytoplasmic proteins in erythrocytes in neurodegenerative pathologies and in reproductive problems (publications 5,6); and hemocyanin and hemocyanin isoforms isolated from garden snails *Helix aspersa maxima* and *Helix lucorum* (publications 7,8,9).

Significantly higher sensitivity and specificity of the thermodynamic parameters of non-secretory type multiple myeloma, in which no monoclonal proteins are secreted, have been demonstrated compared to multiple myeloma with secretion of immunoglobulins IgG and IgM (publications 1,2). The thermodynamic parameters of denaturation of major serum proteins reflect the patients' response to the applied treatment and can be applied for diagnosis and follow-up of patients diagnosed with multiple myeloma (MM) and Waldenström's macroglobulinemia in the course of treatment.

It was found that the calorimetric profiles of blood plasma of experimental animals depend on the sex and age, as well as on the appearance of proliferative lesions and tumors in the intestinal tract of treated animals, and are potential indicators of malignant transformation and progression of tumor formation.

The main proteins of red blood cells - Hb and Band 3 glycoprotein, have higher stability in denaturation for the studied neurodegenerative pathologies (Parkinson's disease, Alzheimer's disease and amyotrophic lateral sclerosis) compared to that in healthy individuals. This effect is more pronounced in the aging process of cells.

In most women who have had a miscarriage, accelerated temperature induced destabilization of red blood cell proteins was found compared to healthy pregnant and non-pregnant women.

It has been shown that the denaturation of hemocyanin from *Helix aspersa maxima* and *Helix lucorum* is an irreversible two-state transition, while two separate transitions have been identified for hemocyanin isoforms purified from garden snails *Helix aspersa maxima*. The denaturation is a kinetically controlled process for all studied forms of hemocyanin.

The non-habilitation publications summarize investigations of the effects of various modifications of hemocyanin (with ferulic, rosmarinic and folic acids) and ionic liquids (containing mono- or dicholinium cations and anions of charged amino acids; choline and non-polar amino acids; based on 1-butyl-3-methylimidazol; cationic amino acid esters and ketoprofen) on its thermal stability and on the viability of breast cancer cell lines (publications 10 -17).

Rapana thomasiana hemocyanin conjugated with ferulic acid has been shown to be prone to aggregation, its temperature stability is not altered, and like native hemocyanin reduces the cell viability of the weakly metastatic, MCF-7, cell line in breast cancer and is not toxic to normal fibroblasts (publications 10,11); rosmarinic acid modification reduces the α -helical structure content and increases the temperature stability of hemocyanins from *Helix lucorum* and *Rapana thomasiana* and does not inhibit the growth of human fibroblasts (publication 12); and modification of hemocyanin from *Helix lucorum* with folic acid does not alter protein stability and has a weak cytotoxic effect on two breast cancer cell lines (MCF-7 and the highly metastatic cell line MDA-MB-231) (publication 13).

Ionic liquids containing mono- or dicholine cations and anions of charged amino acids (Lys, Arg, Asp and Glu) have been shown to induce changes in the secondary structure of *Rapana thomasiana* hemocyanin, except for those containing Glu they do not alter or stabilize hemocyanin, and those containing Arg and Lys exhibit high anti-biofilm activity; choline-based ionic liquids and non-polar amino acid anions significantly affect the secondary structure and temperature stability of hemocyanin from *Helix pomatia*, and their complexes with hemocyanin from *Helix pomatia* show cytotoxicity to the cancer cell line MDA-MB-231; 1-butyl-3-methylimidazolium-based liquids containing acetate, trifluoroacetate or dicyanamide anions prevent aggregation and stabilize the monomeric form of insulin; and ionic liquids composed of cationic amino acid esters and the ketoprofen anion weakly destabilize serum albumin (publications 14-17). These data could be useful in the development of new biocompatible compounds that stabilize proteins in solution and are relevant to biotechnology and biomedicine.

Graphene oxide (GO) has been shown to bind and significantly stabilize albumin (HSA) in isolated state at low ionic strength, whereas the HSA-GO molecular interaction is impaired in blood plasma, indicating that the protein is protected from possible toxic effects of GO under physiological conditions (publication 18).

There is a strong correlation between the change in the thermodynamic behavior of cancer cells (MCF-7 and MDA-MB -231 breast cancer cell lines) and their viability due to the action of the anticancer drugs miltefosine and cisplatin (cis-Pt) (publication 19).

Another group of studies on the effect of PLA1 / A2 polymorphism in the GPIIb / IIIa gene, which is a risk factor for the development of arterial and venous thrombosis, on platelet morphology and nanomechanics in patients with deep vein thrombosis (DVT) showed that the allele carrier PLA1 modulates the state of activation, morphology, and platelet membrane elasticity in DVT patients (publication 21). On the other hand, the carriers of thrombophilic mutations and increased frequency of the polymorphisms (FVL, FII20210A, PLA1 / A2, MTHFR C677T or 4G / 5G PAI-1) of thrombophilia are associated with structural and nanomechanical abnormalities, and increased activation of platelets in women with miscarriages (publications 22, 23).

The main temperature induced transitions of photosynthetic complexes in mutants of cyanobacteria *Synechocystis* sp. PC 6883 and phycobilisomes in intact cells of *Synechocystis* sp. PCC 6803 have been identified (publications 24,25), and the alteration of the thermal stability of the main light-harvesting complex of photosystem II in stacked and unstacked state of the thylakoid membrane have been demonstrated (publication 26).

Prospects for future research Guidelines are presented for future research focused on: molecule-cell interactions and drug-cell interactions; modification / remodeling of type I collagen; application of biophysical approaches to disease diagnosis; study of the effect of synthetic and natural low molecular weight compounds on temperature stability and their interactions with various proteins.

CONCLUSION

The materials presented by Assoc. Prof. Dr. Todinova fully meet and exceed the recommended requirements for holding the academic position "Professor" according to the Law on the Development of Academic Staff in the Republic of Bulgaria (ZRASRB), the Regulations for the Application of ADASRB in BAS and the specific requirements of IBFBMI-BAN.

The scientific production and the high impact / rank of the publications in peer-reviewed journals give a confidence for my positive opinion on the candidacy of Assoc. Prof. Dr. Svetla Zhelyazkova Todinova for the academic position "Professor" and to recommend to the members of the scientific jury and the members of the Scientific Council of IBPhBMI-BAS to elect Assoc. Prof. Svetla Zhelyazkova Todinova for the academic position "Professor" in the professional field 4.3. Biological sciences, scientific specialty: Biophysics.

26.03.2022

/Prof. Stefka Germanova Taneva, DSc/