

STAND POINT

For the competition for election of "Associate Professor" in a professional field 4.3. Biological sciences, scientific specialty "Human Biology" for the needs of the Department "Biology, Medical Genetics and Microbiology" of the Faculty of Medicine of the Sofia University "St. Kliment Ohridski", announced in the State Gazette number 48/28.06.2022.

by Prof. Dr. Antoaneta Vidolova Popova

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member of the Scientific Jury, according to order No. RD 38-500/24.08.2022
of the Rector of Sofia University "St. Kliment Ohridski"

In the announced competition for the academic position "Associate Professor" in the professional field 4.3. "Biological Sciences", scientific specialty "Human Biology" participates only one candidate, Senior Assistant Professor Dr. Lyudmila Filipova Belenska-Todorova. Dr. Belenska-Todorova completed her secondary education in 2000 at II ELS "Thomas Jefferson", Sofia. In 2004, she received a bachelor's degree in "Molecular Biology", and in 2006 defended her master's degree in "Microbiology and Microbiological Control" at the Faculty of Biology of the Sofia University "St. Kliment Ohridski". Dr. Belenska-Todorova has post-graduate diplomas of "Teacher of Biology" from the Faculty of Biology and "Medical Biology" from the Faculty of Medicine of Sofia University. In 2016 Dr. Belenska-Todorova defended a PhD thesis entitled "Role of complement in the processes of joint destruction in experimental models of arthritis" with supervisor Prof. Nina Ivanovska, DSc., and received the educational and scientific degree "doctor" in professional field 4.3. "Biological Sciences", scientific specialty "Immunology", at the Institute of Microbiology, BAS.

From 2008 to 2017, Dr. Belenska-Todorova was an assistant, and after 2017, a Senior Assis. Prof. in "Human Biology" at the Faculty of Medicine of the Sofia University in the Department of "Biology, Medical Genetics and Microbiology". She is leading the compulsory course "Human Biology" in the specialty "Medicine" and "Medicine in English" and the compulsory course "Microbiology, Parasitology and Virology" in the specialty "Nursing" of the Faculty of Medicine of Sofia University. For the period 2008-2019, she had a second employment contract at Lozenets Hospital as a medical specialist in "Medical Biology", and from 2019 she is on a second employment contract (4 hours) in the Laboratory for Molecular Diagnostics, Microbiology, Virology, Parasitology and Genetics in the Faculty of Medicine of SU.

In the current competition for "Associate Professor", Dr. Belenska-Todorova participates with 8 publications in journals referenced in Scopus and Web of Science, with impact factor and quartiles, 7 publications in non-refereed journals, two monographs, one book based on a PhD thesis and 5 book chapters. The total IF of the published articles is 20,701. In 10 of the published papers (5 publications and 5 book chapters), Dr. Belenska-Todorova is the first author, and in 3 she is the last author. According to the ranking of scientific publications by quartiles, the 8 articles of Dr. Belenska-Todorova are as follows – 2 in journals with Q1, 1 in a journal with Q2, 4 with Q3 and one article in a journal without a quartile. Up-to-date topic of Dr. Belenska-Todorova's research is demonstrated by the 37 noticed citations in SCOPUS and Web of Science. The H-factor of Dr. Belenska-Todorova, after excluding self-citations of all authors in SCOPUS, is 3. The results of her investigations have been presented by oral presentations and posters at 13 international and national scientific conferences. She participated in the implementation of 9 national scientific projects, funded by the Ministry of Education and Science, and was the principle investigator of two of them. She was a member of the scientific team of 2 international scientific projects funded by the Ministry of Education and Science and Sofia University. Since 2015, Dr. Belenska-Todorova has been a member of the Commission for evaluation of candidate student works in biology and chemistry for the specialty "Medicine" and "Medicine in English" of the Faculty of Medicine at Sofia University.

A completed reference 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 (ZDASRB) for field of higher education 4. Natural Sciences, Mathematics and Informatics, professional field 4.3. "Biological Sciences", scientific specialty "Human Biology" for the academic position "Associate Professor". According to indicators A and B, the required 50 and 100 points are presented, respectively, according to indicator D – 265 points are presented (required 200) and according to indicator D, 74 are presented (required 50). According to indicator E, 150 points are presented, although they are not required for the academic position "Associate Professor".

A detailed reference of the main achievements, grouped into five topics, of Senior Assis. Prof. Dr. Belenska-Todorova, is also applied. Two of the topics include a significant part of the publications and are in the field of immunology, devoted to analysis of the mechanisms of acute and chronic inflammation. The research has contribution to basic science with the potential for application in clinical practice for the development of rapid and adequate therapeutic approaches.

- A model of septic shock, as an example of acute inflammation, was chosen and the basic cellular and molecular mechanisms involved in its development were analyzed.

- Investigations of chronic inflammation are in the field of osteoimmunology and are directed towards unravelling the role of hormones applied in assisted reproduction procedures in the development of arthrosis.
- Research has been conducted in the field of dermatoglyphics, analyzing the similarities and differences between specific dermatoglyphic patterns on the fingertips and palms of mono- and dizygotic twins.
- A number of reports is devoted to investigation of the anatomical features in humans, which has a significant potential for application in medical practice and especially in the field of surgery.
- The published monographs, the book on the basis of a defended PhD thesis as well as the five book chapters can be used in the educational process of medical students, doctoral students and practicing doctors.

The topic of the monograph "The complement system in inflammatory joint diseases" presented as a habilitation work, is the study of inflammatory joint diseases, which are accompanied by inflammatory processes with different etiology and intensity and loss of bone and cartilage tissue, which can lead to a serious deterioration of the quality of life. Along with the summary of the well-established facts regarding the development of various types of arthritis, the author's original scientific studies on the role of complement in inflammatory joint diseases conducted in animal models of rheumatoid arthritis and osteoarthritis as well as in vitro studies of cell cultures are also included. The available information on the components of the complement system, their receptors, activation pathways and regulatory mechanisms are also systematized. The applied therapeutic approaches for the treatment of inflammatory joint diseases via influencing the activity of complement are also included.

In the second monograph by Dr. Belenska-Todorova "Sepsis", the main factors affecting the development of the phases of sepsis in humans are described, including the role of inflammation, cytokines and complement, as well as the involvement of specific populations of cells interacting with certain co-stimulatory molecules. Special attention is paid to disorders in the functions of immune cells such as tolerance abnormalities and their programmed death. The basic intracellular mechanisms, realized by the participation of the endoplasmic reticulum are described as well. Dr. Belenska-Todorova's research, conducted with a mouse model of sepsis and in vitro studies of cell cultures, has made a significant contribution to unravelling the mechanisms of the development of sepsis and the development of therapeutic strategies for its effective treatment.

In the submitted documents is also included a book based on the successfully defended PhD thesis for obtaining the degree "doctor" - "Role of complement in the processes of joint destruction in experimental models of rheumatoid arthritis". Activation of the complement system has been shown to induce severe synovitis that becomes chronic in a model of erosive arthritis. The periodic complement activation is associated with increased expression of markers of bone destruction. Suppression of expression of the proapoptotic factor TRAIL in joints in the absence of functional complement activity has been established for the first time. New data have been obtained concerning the role of properdin in the development of autoimmune arthritis, which depends on disorders in the alternative pathway of complement activation. The results prove the involvement of properdin in osteoclastogenesis processes. The presented results can be used for the development of criteria for assessing the risk of disease progression and in the creation of new therapeutic approaches based on inhibition of complement activity.

The two published monographs, as well as the published book based on defended PhD thesis of Dr. Belenska-Todorova could be helpful to medical practitioners and immunologists, molecular biologists, pharmacologists, and also in the training of students and specialists.

The scientific contributions in published articles in the world's referenced databases, non-refereed editions and book chapters are grouped into five chapters. A great part of the research of Dr. Belenska-Todorova are original and represent new scientific facts and may also find application for the development of new therapeutic approaches for the treatment of arthritis and sepsis.

1. Immunobiological studies in an experimental model of sepsis with the aim to unravel the molecular and cellular mechanisms of the disease.

The role of apoptosis in the pathophysiology of sepsis has been investigated. It has been shown that blocking of TRAIL (Tumor Necrosis Factor-related Apoptosis-inducing Ligand) at sepsis induction reduces the severity of symptoms mainly by limiting the apoptosis of immune cells in the peritoneum and spleen. New scientific data have been obtained that the expression of TRAIL in the process of sepsis development correlates with high mortality and the development of multiple organ failure syndrome. It has been hypothesized that dendritic cells are targets for apoptotic processes as a result of increased TRAIL expression. New evidence has been obtained that inhibition of functional complement activity limits the development of organ failure in sepsis..

2. Immunobiological studies in experimental models of inflammatory joint diseases for clarification of the mechanisms of bone destruction and remodeling, as well as their systemic nature.

Estradiol has been shown to counteract the inflammation and destruction of cartilage and bone and can be used as an effective agent in the treatment of osteoarthritis. Follicle-stimulating hormone has been shown to stimulate the secretion of pro-inflammatory cytokines, osteoclastogenesis, and to enhance bone destruction, but not to affect osteoblast formation.

On examining the role of the Janus kinase (JAK) inhibitor berberine, its administration was shown to suppress the action of pro-inflammatory cytokines and alleviate joint inflammation. The application of berberine suppresses the increase in the number of megakaryocytes in the bone marrow and could have a preventive effect against the formation of thrombosis in the systemic manifestations of arthritis.

In the investigation of the role of complement in the pathogenesis of arthritis, new data have been obtained showing that when the functional activity of complement is exhausted, a significant relief of synovitis is observed, decreases the expression of bone resorption markers and has a preventive effect against the formation of osteophytes. Absence of serum complement activity at the initiation of arthritis limits proteoglycan loss and affects dectin-1 expression on monocytes and lymphocytes, and that it reduces the number of dendritic cells in the synovial fluid. Possible therapeutic strategies to reduce destructive inflammatory responses in joints during infections have been proposed. Collagenase-induced osteoarthritis has been proposed as a suitable model to study the role of the complement system, sclerostin expression and cellular senescence. The role of megakaryocytes in inflammatory joint diseases, in bone remodeling and in thrombocytosis is also discussed.

3. Investigation of the role of neurogrowth factor NGF in the pathogenesis of myasthenia gravis.

New data on neurogrowth factor expression by mast cells in the thymus in the autoimmune disease myasthenia gravis have been obtained.

4. Study of dermatoglyphic characteristics in mono- and dizygotic twins in order to clarify the influence of the environment on genetic factors in the formation of various diseases, behavior and level of intelligence.

5. Morphological study of emissary openings and veins in the skull.

The results of this study could be applied in imaging diagnostics before surgical interventions.

In conclusion, I believe that the presented documents and scientific indicators as well as the scientific contributions of the published articles and books of Dr. Belenska-Todorova completely fulfill the minimum national requirements for the acquisition of the academic position

"Associate Professor", set in the Law on the Development of the Academic Staff of the Republic of Bulgaria for the field of higher education 4. Natural Sciences, Mathematics and Informatics, professional field 4.3. Biological Sciences, scientific specialty "Human Biology". I strongly recommend the Scientific Jury to propose to the Faculty Council of the Faculty of Medicine at Sofia University "St. Kl. Ohridski" the Senior Assistant Professor Dr. Lyudmila Filipova Belenska-Todorova to be elected as an "Associate Professor" for the needs of the Department of "Biology, Medical Genetics and Microbiology" of the Faculty of Medicine of Sofia University "St. Kl. Ohridski".

10.10.2022 г.

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/Prof. Dr. Antoaneta Popova/