

REVIEW

On: Competition for the occupation of the academic position "Associate Professor" in the Area of Higher Education 4. Natural Sciences, Mathematics and Informatics, Professional Field 4.3. Biological sciences, Scientific specialty "Human Biology", announced by Sofia University "St. Kliment Ohridski", in the State Gazette, number 48/28.06.2022.

by Prof. Tsvetanka Tsankova Marinova, MD, PhD, DMSc, Faculty of Medicine of Sofia University "St. Kliment Ohridski"

Information on the competition procedure

The competition for the occupation of the academic position "Associate Professor" in the professional field 4.3. Biological sciences, Scientific specialty "Human Biology", is announced for the needs of the Department "Biology, medical genetics and microbiology" in the Medical Faculty of Sofia University "St. Kliment Ohridski". The competition announcement was published in the State Gazette, number 48/28.06.2022.

The composition of the Scientific Jury was determined by an Order of the Rector No. RD-38-500 of 24.08.2022 on the grounds of a decision of the Faculty Council of the Faculty of Medicine (Protocol No. 108/23.08.2022).

One candidate participates in the competition: Chief Assistant Lyudmila Filipova Belenska - Todorova, PhD.

The regulatory requirements for the competition procedure have been met. The review was prepared in accordance with the Law on Development of Academic Staff in the Republic of Bulgaria (LDASRB), the Rules for the Implementation of the LDASRB and Section IV-Terms and Conditions for Occupation of the Academic Position "Associate Professor" of the Rules for the Conditions and Procedure for Acquiring Degrees and Occupation of Academic Positions at Sofia University "St. Kliment Ohridski".

The applicant's documents are in compliance with the regulative requirements for admission and participation in the competition for the occupation of the academic position “Associate Professor” at Sofia University “St. Kliment Ohridski“. They are presented in sequence from No. 1 to No. 19 and include supporting evidence: Curriculum Vitae; Higher education diploma (Master's degree and Bachelor's degree); Diploma for educational and scientific degree “Doctor”; Diploma for medical specialty in “Medical Biology”; Document for academic position “Chief Assistant”; Certificate for work experience in the specialty; Reference to the indicators under art. 112, para 2; List of scientific publications (a list of all publications and a list of publications submitted for participation in the competition); List of participations in scientific forums; List of participations in projects; Reference according to the form for meeting the national minimum requirements for holding the academic position "Associate Professor" with evidence; Reference of citations; Reference to original scientific contributions; Scientific papers submitted for participation in the competition; Summaries of peer-reviewed publications in Bulgarian and English; Copy of the announcement in the State Gazette; Other documents and materials about the candidate's activity.

Applicant's curriculum vitae and academic development

Chief Assistant Lyudmila Belenska, PhD was born in 1982 in Sofia. She obtained a Master degree in “Molecular Biology” at the Faculty of Biology, Sofia University “St. Kliment Ohridski” with professional qualification "Molecular Biologist - Master of Microbiology and Microbiological Control" (Diploma Series A - 2005 SU No. 180108; Reg. No. M 180108/13.03.2006 and professional qualification "Biology Teacher" (Diploma No. SU 000583; Reg. No. 8450/16.04.2007, Faculty of Biology, Sofia University “St. Kliment Ohridski”).

In 2014 she acquired a medical specialty in Medical Biology (Diploma SU No. 000004 of May 16, 2014). She was awarded the educational and scientific degree “Doctor” in 4.3. Biological sciences (Immunology) in 2016 (Diploma No. 000735/01.07.2016 г.) of the Institute of Microbiology, Bulgarian Academy of Sciences).

Lyudmila Belenska has been working consecutively as an Assistant in Human Biology (20.08.2008 – 30.07.2017) and a Chief Assistant in Human Biology (from 31.07.2017 until present) in the Department “Biology, medical genetics and microbiology”, Medical Faculty of Sofia University “St. Kliment Ohridski”.

She performs in good faith and dedicatedly various types of educational, administrative, organizational and expert activities at the Faculty of Medicine of Sofia University “St. Kliment Ohridski” as well as activities as a medical specialist and technical assistant in Medical Biology (from 2008 until present) at UB "Lozenets" and Faculty of Medicine of Sofia, University “St. Kliment Ohridski“ (Laboratory for molecular diagnostics, microbiology, virology, parasitology and genetics). Chief Assistant Lyudmila Belenska has specialized abroad: Faculty of Medicine of the University of Cologne, Germany (21.06.2010 – 11.07.2010) and Tor Vergata University, Rome, Italy (7 - 12.06.2009). Dr. Lyudmila Belenska is a member of three expert commissions and two scientific organizations. She is a mother of two children.

Scientific research and scientometric data

The applicant's scientometric data, evaluated in their wholeness, are in full compliance with the criteria and indicators recommended in the regulations for evaluation by the Scientific Jury at conducting a competition for “Associate Professor”. The scientific papers submitted for review are from the field of higher education 4. Natural Sciences, Mathematics and Informatics, professional field 4.3. Biological sciences, Scientific specialty “Human Biology”.

Chief Assistant Lyudmila Belenska is the author of published and reported scientific papers with significant contribution in the field of *Medical biology*.

Her dissertation for the award of the educational and scientific degree "Doctor" is on the topic: “Role of Complement in the Processes of Joint Destruction in Experimental Models of Arthritis”, Sofia 2016, with supervisor Prof. Nina Ivanovska, PhD, DSc. The experimental research of the dissertation was conducted at the Institute of Microbiology, Bulgarian Academy of Sciences.

The total scientific production presented by Chief Assistant Dr. Lyudmila Belenska includes: published scientific articles - 27 (among them, 11 publications in journals with impact factor and Q rank/quartile according to the SJR; 4 publications related to the dissertation); monographs – 2, book based on the dissertation work – 1, book chapters – 5; reported scientific papers in international and national scientific forums – 19 (6 - related to the dissertation).

Dr. Lyudmila Belenska has participated in 11 research projects (international projects – 2; project manager – 2). According to the information provided the total IF is 27.103, and the individual IF is 2.71.

For her participation in this competition, Chief Assistant Dr. Lyudmila Belenska has presented: 23 scientific articles, 8 publications of them being internationally referenced and indexed in the international databases Scopus and Web of Science of journals with IF, 7 in peer-reviewed journals; monographs – 2; book based on dissertation work – 1; book chapters – 5; participation in scientific conferences and congresses - 13, which are not peer-reviewed in previous competitions for awarding scientific degrees and academic positions.

Dr. Lyudmila Belenska has participated in 11 research projects (international projects – 2; project manager – 2). The total IF is 20.61 and individual IF is 1.171.

The *H-index* of Lyudmila Belenska is 3 - according to the data from Scopus, 3 - according to the data from Web of Science and 4 - according to Google Scholar. According to the information provided, 37 citations are found in the *Scopus* and *Web of Science* databases (without self-citations) and 14 more according to Google Scholar.

Analysis of scientific contributions

The scientific interests of Chief Assistant Dr. Lyudmila Belenska and the published scientific results are in the field of the announced competition.

The most significant results from the scientific work of Dr. Lyudmila Belenska are reflected in detail in the "Author's reference for the contributory nature of scientific works" attached to the documents of the competition. They are in several fields: medical

biology, immunology, molecular and cellular biology, dermatoglyphics, medical pedagogy, comparative anatomy, and have theoretical and medico-biological applications. A significant part of the scientific works are in the field of immunobiology (osteimmunology, infectious immunology) and are aimed at analyzing the mechanisms of acute and chronic inflammation.

The most significant original scientific contributions, reflected in the scientific works of Chief Assistant Dr. Lyudmila Belenska can be systematized in five scientific directions:

1. Immunobiological studies in experimental models of inflammatory joint diseases

1.1. A monograph (habilitation thesis) is presented on the topic "The complement system in inflammatory joint diseases", Lyudmila Belenska-Todorova, University Publishing House "St. Kliment Ohridski", Sofia, 2019, ISBN: 978-954-07-4652-4 (publication no. V.1).

The monograph analyzes the role of complement in some inflammatory joint diseases: rheumatoid arthritis, osteoarthritis, juvenile idiopathic arthritis, ankylosing spondylitis, septic and psoriatic arthritis. The components of the complement system, their receptors, activation pathways and regulatory mechanisms are described. Approaches to the treatment of inflammatory joint diseases by influencing complement activity are also summarized.

Various experimental models of arthritis have been developed in order to better study joint diseases and achieve their more effective treatment. Research is aimed at studying the role of the complement in animal models of rheumatoid arthritis and osteoarthritis. More commonly used are a murine model of zymosan-induced rheumatoid arthritis (ZIA) induced by an intra-articular injection into the ankle joint cavity with zymosan A obtained from the yeast *Saccharomyces cerevisiae* and a murine model of collagen-antibody induced arthritis (CAIA). *In vitro* studies were also performed on cell cultures obtained from arthritis models in view of the observed effect of determining factors on terminal differentiation. The monograph can be useful in the training of students, specialists, doctoral students and specialists from various fields.

1.2. A book is presented and published on the basis of a protected dissertation work for PhD on the topic "Role of complement in the processes of joint destruction in experimental models of rheumatoid arthritis", Lyudmila Belenska - Todorova, University Publishing House "St. Kliment Ohridski", Sofia, 2018, ISBN: 978-954-07-4651-7 (publication No. IV.1).

Rheumatoid arthritis (RA) is a chronic inflammatory joint disease characterized by severe synovitis and destruction of bone and cartilage. The exact mechanisms for the development of RA are not yet fully understood, as they are complex and include genetic predisposition, environmental factors, and immune dysregulation.

This edition summarizes the results of a dissertation work in professional field 4.3. Biological sciences, scientific specialty "Immunology" (06.01.23). The effect of the complement on different cell populations and mediators of bone destruction was analyzed in two models of rheumatoid arthritis: zymosan-induced arthritis and collagen-antibody-induced arthritis. The described dissertation work was carried out under the supervision of Professor Nina Ivanovska, PhD, DSc. In the synovium of patients with RA, the presence of activated components of the complement system has been demonstrated, which probably play an important role in the pathogenesis of this disease and tissue destruction.

1.3. Effect of estradiol and follicle-stimulating hormone on apoptosis, inflammation and destruction of bone and cartilage in a mouse model of collagenase-induced osteoarthritis (OA).

Original results have been obtained on the effect of 17β -estradiol (ED) and follicle-stimulating hormone (FSH) on bone marrow (BM) cell differentiation in arthritic mice. The conclusion of the conducted research is that both hormones have an impact on the differentiation of BM cells, with FSH supporting the formation of osteoblasts and ED - the accumulation of osteoblasts. (publications I.1; I.4; I.6)

1.4. Role of the Janus kinase (JAK) inhibitor berberine in inflammatory joint disease

Berberine is a protoberberine alkaloid with a wide spectrum of pharmacological activity and is considered to be an inhibitor of Janus kinases (JAK). The mechanism of

action of berberine in inflammatory joint diseases has not yet been clarified. The effect of berberine on apoptosis and the formation of senile cells has been demonstrated for the first time.

Berberine reduces the formation of apoptotic and senile cells in bone marrow and bone, as well as the formation of TRAIL-induced osteoclasts. The alkaloid did not change the expression of the anti-apoptotic factor Bcl-2 and increased the expression of the pro-apoptotic factor Bax in synovial cells. Berberine limits the accelerated formation of apoptotic and senile cells in mice with arthritis, which could have an alleviating effect on joint inflammation. (publications II.1, II.4, III.3)

1.5. Role of complement in the pathogenesis of osteoarthritis (OA)

Complement activation is an integral part of many autoimmune and inflammatory diseases, including OA. It is involved in the pathogenesis of chronic synovitis in human rheumatoid arthritis (RA). Original data are presented for depletion of functional complement activity at the time of initiation of zymosan-induced arthritis, significant downregulation of TGF- β 1/3, BMP2, and pSmad2 expression, and reduction of Sudan black B-positive cells in the synovium. The lack of functional complement prevents the development of chronic synovitis, the formation of osteophytes and the formation of pathological senile arthritic cells.

New data have been obtained on the effect of the substances metformin and alendronate, as well as their combination, on the development and progression of OA in mice with collagenase-induced osteoarthritis (KIOA).

Obesity is considered a major risk factor for the development and progression of osteoarthritis (OA) of the knee. Serum levels of leptin and resistin were measured and analyzed in knee OA patients with different body mass index values. The obtained data support the hypothesis that the presence of obesity is a prerequisite for the earlier development of knee OA as an isolated localization of the disease in younger patients before the appearance of osteoarthritic changes elsewhere in the body. (publication I.7; III.1; III.2; III.5)

1.6. Role of megakaryocytes in inflammatory joint diseases

Original data are presented that megakaryocytes and platelets have a key role in joint inflammation, bone remodeling and in accompanying systemic disorders such as thrombocytosis. (publications II.2; III.3; III.4)

2. Immunobiological studies in an experimental model of sepsis

2.1. A monograph on "Sepsis" is presented. (Lyudmila Belenska-Todorova, "St. Kliment Ohridski" University Publishing House, Sofia, 2021, ISBN: 9789540751634); (publication V.2).

The monograph describes the main factors influencing the development of the phases of sepsis in humans, including the role of inflammation, cytokines and complement, as well as the involvement of specific populations of cells interacting with certain costimulatory molecules. Special attention is paid to disorders in the functions of immune cells such as tolerance abnormalities and their programmed death.

New data are presented on the role of apoptosis in a mouse model of sepsis induced by an intraperitoneal injection of zymosan A (a component of the cell wall of the yeast *Saccharomyces cerevisiae*), which leads to generalized inflammation resembling human septic shock.

Absence of serum complement activity was found to reduce the number of pro-inflammatory immune cells and suppress zymosan-induced organ failure by limiting liver damage and altering liver enzyme levels. The obtained results indicate that the inhibition of the functional activity of complement would find application in therapeutic approaches to limit the development of organ failure in sepsis. The monograph could serve the purposes of teaching students, specialists and doctoral students.

2.2. Exploring the role of apoptosis in the pathophysiology of sepsis and searching for a strategy to influence it

Data are presented on the consequences of blocking tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) in a murine model of zymosan-induced septic shock. It was found that blocking TRAIL at the time of sepsis induction could reduce the severity of symptoms mainly by suppressing the accelerated apoptosis in the peritoneal exudate and spleen. (publications I.4; II.5)

2.3. Exploring the role of complement in the mechanisms of sepsis

Low complement activity at the time of initiation of septic shock in experimental mice was found to increase survival, prevent liver enlargement, and reduce the rise in serum markers of liver injury at 48 hours. Apoptosis in the PE and spleen was suppressed in the complement-depleted animals, and IL-6 levels in the PE and spleen were limited. The clinical correlations of the obtained results are discussed (publication II.3).

3. Immunobiological studies in autoimmune diseases

New structural and immunocytochemical data were obtained on the expression of some growth factors (NGF, IGF-I) and their receptors in the thymus of healthy individuals and patients with myasthenia gravis. The role of immunopositive stromal cells and Hassall's bodies in T-cell ontogeny, positive and negative selection of thymocytes, and myasthenic transformation of the thymus is discussed. (publication II.7; VI. 9, 10, 11, 12, 13).

4. Study of dermatoglyphic characteristics in mono- and dizygotic twins

Qualitative analysis of palms and fingerprints of twins was conducted. New data have been obtained on the characteristics of dermatoglyphic patterns in monozygotic and dizygotic twins. (Publication I.8 and II.6).

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

Several anatomically significant variants of the occipital emissary foramina and veins have been described. Their evolutionary and clinical significance is discussed. (publication I.5)

Chief Assistant Lyudmila Belenska, PhD is registered in the Register of Scientific Activity at NACID. The comparative analysis of the minimum national requirements under Art. 2b of the Law on Higher Education in the field of higher education 4. Natural sciences, mathematics and informatics, Professional field 4.3. Biological Sciences with the attached reference to the real points of the candidate shows that Lyudmila Belenska meets the minimum national requirements for holding the academic position of "Associate Professor".

The detailed analysis of the relevant groups of indicators **A/A**, **B/Б**, **C/В**, **D/Г**, **E/Д**, **F/E** of Dr. Belenska proves the following: Indicators **A** – 50 points (required 50 points) and **C** [C.3] - 100 points (required 100 points) meet the national requirements. Indicator **D** is 265 points at a minimum requirement of 200. Indicator **E** is 74 points at a minimum requirement of 50. (Total number – 489 points for A - E). Indicator **F** is 150 points with a minimum required value of 0 points for academic position "Associate Professor". The total number of points of Dr. Belenska is 639 with the minimum number as a national requirement for the academic position of "Associate Professor" being 400 points. By groups of indicators (**D**, **E** and **F**). Dr. Belenska's values exceed the national minimum requirements.

Teaching and lecturing activities

Chief Assistant Lyudmila Belenska is a lecturer with intensive teaching work in the field of *Medical Biology*. She has significant experience in teaching "*Human Biology*" to students for the educational qualification degree Master, specialty Medicine in Bulgarian and English and in the subject "*Parasitology*" to students with a Bachelor's degree "Nurse". The report on the study employment of Dr. Belenska shows that her classroom employment in the discipline "Human Biology" with students in "Medicine" and the discipline "Parasitology" with students in "Nurse" at the Faculty of Medicine is over 4500 hours.

She actively participates, including as deputy chairman of the examination committee, in the preparation, conduct and evaluation of candidate student examination papers in Biology and Chemistry in Bulgarian and in English for students majoring in Medicine of the Medical Faculty of Sofia University "St. Kliment Ohridski".

Chief Assistant Lyudmila Belenska is respected by her students and colleagues as a highly qualified and erudite teacher.

Conclusion

Chief Assistant Lyudmila Filipova Belenska - Todorova, PhD, participating in the competition for the occupation of academic position of "Associate Professor" is a very hardworking and established researcher with significant scientific work and original contributions in the field of medical biology, immunology, molecular and cell biology. She is a highly respected lecturer in *Human Biology*, a highly qualified specialist with excellent team research work.

Lyudmila Belenska, PhD shows responsibility, discipline, motivation, consistency, perseverance, competence and precision in all aspects of her research and teaching activity. Her research work is intensive and productive. Dr. Belenska's scientometric data are not only in compliance, but also exceed the national minimum requirements, the regulative criteria and indicators for evaluation of candidates in conducting a competition for the academic position "Associate Professor".

In general, the original scientific results obtained by Lyudmila Belenska, PhD have an indisputable fundamental and scientifically applied contribution character in the medico-biological aspect, with possibilities for application in the medical practice.

The complex evaluation of her documents gives me grounds for a positive opinion. Therefore, with complete conviction, I propose to the honourable members of the Scientific Jury to decide on the election of Chief Assistant Lyudmila Filipova Belenska - Todorova, PhD for "Associate Professor" in professional field 4.3. Biological Sciences, scientific specialty "*Human Biology*" and occupation of this academic position at the Department "Biology, medical genetics and microbiology" in the Medical Faculty of Sofia University "St. Kliment Ohridski".

01.10.2022

Sofia

Member of the Scientific Jury:

(Prof. Ts. Marinova, MD, PhD, DMSc)