

## STATEMENT OF ACADEMIC OPINION

By Prof. Dr. Boryana Varbanova, MD

Medical University "Prof. Dr. Paraskev Stoyanov" Varna

Department of Pediatrics

Regarding thesis for obtaining of the educational and scientific degree of "Doctor" in the field of higher education 7. Healthcare and sports, professional direction 7.1. Medicine, doctoral program "General Medicine"

**Author:** Dr. Irina Ivanova Momcheva

**Form of doctoral studies:** correspondence

**Department:** Department of General Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" Varna

**Topic:** Study of the involvement of humoral factors of innate immunity in the pathogenesis of activated osteoarthritis

**Supervisor:** Assoc. Prof. Dr. Zhenya Ruseva, MD, Department of General Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" Varna

### General presentation of the doctoral student and the procedure:

Dr. Irina Ivanova Momcheva was born on April 14, 1967, in Sredets. She completed her medical education at the Medical University of Plovdiv in 1993. From 1993 to 1998, she worked as a therapist in outpatient practices in the Burgas region. From 2000 to 2008, she was a general practitioner at the "Medika 2000" group practice in Burgas. She specialized in rheumatology at the Clinic of Rheumatology at the University Multiprofile Hospital "St. Marina" Varna from 2008 to 2010. From 2010 until now, she has been working as a rheumatologist in the Rheumatology Department of the University Multiprofile Hospital in Burgas. Since 2021, she has been an assistant professor of Propaedeutics of Internal Diseases and Rheumatology at the Faculty of Medicine of the University "Prof. Dr. Assen Zlatarov" Burgas. She has acknowledged specialty in internal medicine and rheumatology. She has completed a degree in Business Administration and Health Management at the University "Prof. Dr. Assen Zlatarov" Burgas.

Dr. Momcheva is actively engaged in scientific research with participation in scientific congresses and symposia and publications in the field of rheumatology.

Thesis documents are prepared in accordance with the regulatory requirements for the award of the educational and scientific degree of "Doctor," and the procedure is approved by the Rector's Order of the Medical University "Prof. Dr. Paraskev Stoyanov" No. R-110-69/26.02.2024.

**Relevance of the topic:**

Osteoarthritis is the most common joint disease in adults, known to medicine since antiquity. The first scientific descriptions date back to the 19th century. However, only in the last few decades have pathogenetic inflammatory mechanisms been proven, which positioned this condition beyond its status as a degenerative age-related condition. The medical significance of expanding knowledge in this area is important, on one hand, due to the widespread impact on the aging population, and on the other hand, the increase of mean life expectancy and the need to improve the quality of life. Despite numerous studies, a unified universal approach evaluating the current state of the inflammatory process, predicting its clinical course, and responding to treatment, is still not widely accepted. The establishment of reliable, easily implementable, economically effective, and validated biomarkers for osteoarthritis still awaits its practical realization.

**Competence on the issue:**

In the literature review, Dr. Momcheva demonstrates in-depth theoretical knowledge. The anatomy and molecular structure of the joint apparatus in osteoarthritis, particularly of the knee joint, are discussed in detail. Emphasis is placed on the role of low-grade inflammation of the synovial membrane in exacerbations of osteoarthritis and its consequences for the structural and functional disorganization and remodeling of the underlying tissues - cartilage and bone. The importance of proinflammatory cytokines in the pathogenesis of osteoarthritis is highlighted. The function of adipokines and inflammatory mediators from the arachidonic acid cycle are discussed skillfully. The significance of the mechanisms of the innate immune response in the pathogenesis of osteoarthritis is pointed in detail. Of particular interest is the involvement of TLRs, complement fractions, and metalloproteinases. Special attention is paid to the complement cascade and its role in the inflammatory processes of osteoarthritis, which is also the leitmotif of the scientific work.

**Characterization and evaluation of the thesis and contributions:**

The thesis is well-structured and is the personal achievement of the author. Presented in 120 pages, distributed as follows: literature review, hypothesis, aim and objectives, materials and methods, results, discussion, conclusions, contributions, publications and communications, scientific applications, and bibliography. The thesis includes 24 numbered tables, 18 numbered graphs, and 6 histograms, all well-designed. Some tables are in English, which could have been avoided. Unnumbered tables and diagrams are also noticed in the text. The bibliography includes 237 sources from foreign and Bulgarian authors.

The aim of the thesis is clearly formulated, and the six tasks are logical and comprehensive.

The material includes 156 patients aged between 43 and 90 years, meeting the ACR criteria for knee osteoarthritis. Of these, 121 are women and 35 are men. The selected patients have activated osteoarthritis of the knee joint in the absence of anamnestic, clinical, and laboratory data for another condition that could be a cause of effusion, based on properly selected exclusion criteria. The levels of C3 and C4 complement fractions and CRP in serum and synovial fluid were examined using a turbidimetric method. The results were processed using appropriate statistical methods with the help of SPSS.

Results and discussion: The demographic characteristics of the patients - gender and age, were analyzed sequentially. The levels of C3, C4, and CRP are presented both in serum and synovial fluid. The comparative analysis shows significantly higher levels of these indicators in the serum of the studied patients. The values of the three studied proteins in synovial fluid are on average 42.14% for CRP, 34.90% for C3, and 30.97% for C4 of their values in blood plasma, with norms ranging from 10% for complement levels to 20% for CRP levels in a healthy joint. The obtained results correspond to those published in the literature. A correlation with the radiological stage of the disease was sought. There is no trend for increase of inflammation in radiologically more advanced osteoarthritis. Relatively higher levels are found in early radiological stages, which the author explains by more pronounced repair processes during this period. A visual schematic model of inflammation in osteoarthritis, suitable staging, and justified therapeutic strategy including anti-inflammatory treatment along with other pharmacological and non-pharmacological methods known in clinical practice are proposed. Future innovative strategies for anti-inflammatory therapy in osteoarthritis are discussed. Potential candidates for future targeted therapy are indicated.

The conclusions are logical and derive from the established results.

The contributions of the thesis are correctly formulated and objective.

In connection with the dissertation, Dr. Momcheva has presented 3 scientific articles and participated in 3 congresses and conferences.

The presented abstract corresponds in content and format to the requirements.

**Conclusion:** The thesis of Dr. Irina Ivanova Momcheva on the topic "Study of the involvement of humoral factors of innate immunity in the pathogenesis of activated osteoarthritis" is an original issue on a current subject with original scientific and practical contributions, fully meeting the requirements of the Regulations of the Medical University "Prof. Dr. Paraskev Stoyanov" Varna for the conditions and procedure for acquiring scientific degrees. I recommend to the honorable members of the jury to award the educational and scientific degree of "Doctor" in the professional field of Medicine, doctoral program "General Medicine" to the doctoral candidate.

19.03.2024

Заличено на основание чл. 5,  
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Prepared the opinion:

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