OPINION

By assoc. prof. Maria Dimova, MD, PhD

Refers to: PhD work in the specialty "Internal Medicine", professional field 7.1 Medicine, field of university education 7. Health and Sports, in accordance with the Order \mathbb{N}_{2} P – 109-218/25.05.2022 of the Rector of Medical University "Prof. Dr. Paraskev Stoyanov "- Varna

Topic: The role of necroptosis in inflammatory bowel disease

PhD student: Elena Panayotova Panayotova, MD - PhD student at the

Department of Propaedeutics of Internal Medicine, MU-Varna

Accademic mentor: Assoc. Prof. Antonia Yordanova Atanasova, MD, PhD Ds

1. Presentation of the procedure

This opinion has been prepared in accordance with the requirements of the Regulations on the structure and activity and the Regulations for the development of academic staff of MU-Varna and the Law on the development of the academic staff of the Republic of Bulgaria.

The presented set of materials on paper and electronic media is in accordance with the Procedure for Acquisition of PhD at MU-Varna.

2. Brief biographical reference

Dr. Elena Panayotova Panayotova was born in 1978 in Ruse. In 2004 she graduated with a degree in Medicine from the Medical University of Sofia. She has specialty "Internal Medicine" since 2014, and in "Gastroenterology" since 2020.

Dr. Panayotova began her professional development in 2005 at the University Hospital "Alexandrovska" - Sofia, and in 2009 she moved to the University Hospital "St. Marina" - Varna, where she works ever since.

Dr. Panayotova's career as a lecturer at the Medical University of Varna began in 2013 as a part-time lecturer, and since 2017 she has been a full-time assistant at the Department of Propaedeutics of Internal Medicine.

3. Relevance, significance of the topic

Inflammatory Bowel Disease (IBD) is an increasingly common disease that mainly affects young people, and their lifelong evolution leads to significant gastrointestinal dysfunction with subsequent severe damage. A distinctive feature is the recurrent inflammation of the intestinal mucosa, which can affect different parts of the gastrointestinal tract. Clinically, they alternate between periods of remission and relapse, which have different durations, and phases of activity often lead to local and systemic complications. This worsens the quality of life of patients, requires long-term treatment and is associated with significant socio-economic costs.

Despite advances in medicine, the etiology and pathogenesis remain unclear, creating diagnostic and therapeutic difficulties for health professionals. Recent experimental studies have identified a new type of cell death in the intestinal epithelium called necroptosis, which leads to inflammation, with characteristics similar to inflammatory bowel disease. This suggests its involvement in the pathogenesis of these diseases.

More research is needed to clarify the role of necroptosis in inflammatory bowel disease. Deciphering key molecules involved in necroptosis cell death would not only provide new diagnostic approaches, but would also contribute to more effective treatments.

4. Structure of the PhD

The work I got acquainted with proves the existence of a clearly defined profile of scientific interests, specific scientific tasks and working hypotheses.

The presented scientific work is written on 166 standard pages and is illustrated with 16 tables, 90 figures and 2 photos. The literature includes 283 literary sources, of which 9 in Cyrillic and 274 in Latin. The coverage of Bulgarian sources is of special significance. The literary review is detailed and extensive and is entirely topic-oriented. It covers all aspects of the given topic and logically presents the arguments for undertaking the research. Dr. Panayotova's good scientific training and knowledge on the problem is made evident through it.

The aim of the PhD is formulated specifically, clearly and precisely in the direction of analyzing the expression of the marker of necroptosis in patients with inflammatory bowel disease.

To achieve this goal, 5 tasks have been set, which derive from it and allow the comprehensive development of the study.

Material and methods. The design of the study is presented on 14 pages and is built according to the objectives of the work.

The number of observation units 170 is sufficient for statistical analysis.

The study is retrospective, as the participants included in the study are patients diagnosed with Crohn's Disease (CD) and Ulerative collitis (UC) according to the criteria of the ESSO.

Complete medical records as well as biopsy material are available for each patient. The medical documentation of each patient was examined in detail and anamnestic, clinical, laboratory, imaging, endoscopic and morphological data were collected and used in the analyzes. All methods used in this study are described in detail.

The results and the discussion cover 68 pages and follow the sequence of the set tasks. They are presented systematically, illustrated with figures and tables, and there is no overlap of the information that the latter presents. The author

comments analytically on the results obtained, comparing with the data obtained by other Bulgarian and foreign researchers.

The formulated 11 conclusions correspond to the results and cover the overall scientific research.

The PhD student has identified 9 contributions, divided into three groups: theoretical, practical and original.

5. Assessment of the publications and personal contribution of the doctoral student.

The PhD student has presented 5 publications in Bulgarian journals, of which 3 are full-text and 2 are abstracts and 2 participations in scientific forums related to the dissertation, all of them in the first author.

6. Abstract

The content and quality of the abstract corresponds to the developed work and is made according to the requirements of MU-Varna. Reflects the main results achieved in the dissertation, the conclusions and contributions.

7. Remarks

I have no critical remarks on the research and the materials presented.

CONCLUSION

The PhD I got acquainted with shows that the PhD student Dr. Panayotova has in-depth theoretical knowledge and professional skills. She demonstrates qualities and abilities to conduct research independently.

The PhD work contains scientific and applied results, which represent an original contribution to science and meet the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria, the Regulations for the implementation of the low and the Regulations of MU-Varna.

All the above gives me the reason to strongly support Dr. Elena Panayotova Panayotova, believing that there is every reason to award her educational and scientific degree "PhD", as well as to recommend to the distinguished members of the scientific jury to vote positively for it answer.

2.06.2022

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