

## REVIEW

From Prof. Dr. Vanya Alexandova Gerova – Nankova, PhD  
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By Order № P-109-218 / 25. 05. 2022 of the Rector of the Medical University of Varna I was elected a member of the Scientific Jury, and on the basis of Protocol №1 / 26. 05. 2022 I was appointed to prepare a review under the procedure for awarding the educational and scientific degree "Doctor" with a candidate:

**Dr. Elena Panayotova Panayotova** - Department of Propaedeutics of Internal Medicine, Faculty of Medicine, Medical University of Varna

**Topic:** "The role of necroptosis in inflammatory bowel disease"

**Field of higher education:** 7. "Health and Sports" in professional direction 7.1. "Medicine" and the scientific specialty "Internal Medicine"

**Research Supervisor:** Assoc. Prof. Dr. Antonia Yordanova Atanassova, MD, PhD, Dsc

### **1. General presentation of the procedure and the PhD student**

The presented set of materials on paper and electronic media has been properly prepared in accordance with the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for its application and the Regulations for the development of the academic staff of MU-Varna.

Includes the following documents:

- Application to the Rector of MU-Varna for opening a procedure for defense of the dissertation
- Autobiography signed by PhD student
- A copy of the diploma of higher education
- A copy of diplomas for the specialty
- Orders for enrollment and deduction with the right of defense
- Protocols of completed doctoral minimum in specialty and language
- Protocol of the Department Council held for preliminary discussion of the dissertation and decision to disclose the procedure and members of the scientific jury

- Dissertation work
- Abstract of a dissertation
- List of scientific publications and participations on the topic of the dissertation
- Declaration of originality and authenticity of the attached documents

The PhD student has attached 3 full-text publications in the publications of MU-Varna.

## **2. Brief biographical data about the PhD student**

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 acquired the specialty "Internal Medicine" in 2014, and in 2020 - the specialty "Gastroenterology". Dr. Panayotova began her professional development as a physician in 2005 at the University Hospital "Alexandrovska" - Sofia, and since 2009 she has worked at the University Hospital "St. Marina" - Varna until present. Dr. Panayotova's career as an assistant at the MU-Varna began in 2013 as honorary assistant and since 2017 she has been a full-time assistant at the Department of Propaedeutics of Internal Medicine.

## **3. Relevance of the topic and expediency of the set goals and tasks**

Inflammatory Bowel Disease (IBD) are diseases of increasing frequency; they mainly affect young people of active creative age, and their lifelong evolution leads to significant impairment of gastrointestinal function with subsequent severe impairment. A distinctive feature is the recurrent inflammation of the intestinal mucosa, which can affect different parts of the gastrointestinal tract. The chronic course of IBD, possible complications, the need for long-term treatment, sometimes with more powerful drugs and the risk of additional side effects, etc., worsen the quality of life of patients and negatively affect their social activity and performance, which is associated with significant socio-economic costs.

Despite intensive research, the etiology and pathogenesis of IBD remain unclear, creating diagnostic and therapeutic difficulties for healthcare professionals.

In recent years, much evidence has accumulated to support the key role of impaired intestinal barrier function as a primary, genetically determined defect in the onset and persistence of intestinal inflammation in IBD.

In order to ensure the structural integrity and stability of the mucosal barrier, it is necessary that cell death of intestinal epithelial cells be strictly regulated. 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 IBD. This suggests its involvement in the pathogenesis of these diseases.

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

The aim and tasks of the dissertation are clearly and precisely formulated.

#### **4. Knowledge of the problem**

The PhD student Dr. Elena Panayotova knows perfectly the state of the problem and creatively evaluates the literary material. Evidence of this is the detailed literature review, prepared on the basis of a total of 283 literary sources, of which 9 in Cyrillic and 274 in Latin, richly illustrated with figures and photographs.

#### **5. Research methodology**

The selected research methods allow achieving the set goal and obtaining an adequate answer to the tasks solved in the dissertation.

#### **6. Characteristics and evaluation of the dissertation**

The dissertation of Dr. Elena Panayotova is structured according to the procedural requirements. It contains 166 standard pages and is illustrated with 16 tables, 90 figures and 2 photos.

The literature review is detailed and well structured. It is written competently and clearly on 39 pages. The style of the exhibition is accurate and shows a good language and medical culture. The analysis at the end of the review reflects the unresolved issues on the problem and logically justifies the need and motivation for the development of the dissertation.

The goal and the set 5 tasks are in accordance with the chosen topic. The research hypothesis is well formulated.

The retrospective study included 170 patients over 18 years of age diagnosed with IBD (of which 85 patients with Crohn's disease and 85 with ulcerative colitis), as well as 30 healthy controls passed through the structures of the University Hospital "St. Marina - Varna for the period from 2011 - 06.2020.

The results are systematized and arranged according to the tasks in 6 subsections of 60 pages. Visualization is at the required level.

The discussion was conducted according to the modern requirements for structuring a dissertation, separately for each task. It is written competently and argumentatively, based on one's own results, in comparison with the literature data. The citations are correctly marked. Tables and graphs obtained after statistical data processing are attached.

The conclusion and the 11 conclusions formulated are directly related to the obtained results.

The contributions reveal the modern orientation of scientific work.

## **7. Contributions and significance of development for science and practice**

The contributions of the dissertation of Dr. Panayotova are systematized and divided into three groups: theoretical, practical and original. Of the greatest interest are the original contributions:

1. For the first time nationally, study of the nuclear expression of RIPK3 in patients with IBD has been performed.

2. For the first time nationally and globally, the relationship between RIPK3 expression and the clinical and endoscopic activity of IBD patients has been demonstrated.

3. For the first time nationally and globally the role of RIPK3 expression as a marker for differentiating IBD patients has been studied.

4. For the first time nationally and globally RIPK3 expression has been evaluated as a prognostic marker for the development of severe disease and progression.

## **8. Evaluation of the dissertation publications**

Publications and participations in scientific forums are distributed as follows: 3 full-text publications, 2 abstracts and 2 participations in scientific forums. In all of them, Dr. Panayotova is the first author.

## **9. Personal participation of the PhD student**

In my opinion, the personal participation of the PhD student Dr. Panayotova in the dissertation research is indisputable and the formulated contributions and results are the personal merit of Dr. Panayotova and her supervisor Assoc. Prof. Dr. Antonia Yordanova Atanassova, MD, PhD, Dsc.

## **10. Abstract**

The abstract of Dr. Panayotova is prepared according to the procedural requirements and reflects the main results and scientific contributions to the dissertation.

### **11. Critical remarks and recommendations**

I have no critical remarks on the final version of the dissertation. I recommend Dr. Panayotova to continue her work in the field of research on the relationship between necroptosis and inflammatory bowel disease.

### **CONCLUSION**

The dissertation contains scientific, scientific-applied and applied results, which represent an original contribution to science and meet all the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria, the Regulations for its application and the Regulations of MU-Varna. The presented materials and dissertation results completely correspond to the specific requirements of MU-Varna.

The dissertation shows that the PhD student Dr. Elena Panayotova has in-depth theoretical knowledge and professional skills in the scientific specialty "Internal Medicine" by demonstrating qualities and skills for independent research.

Due to the above, I convinced give my positive assessment of the research presented in the dissertation, abstract, results and contributions and propose to the esteemed scientific jury to award the educational and scientific degree "Doctor" of Dr. Elena Panayotova Panayotova.

Date: 01.06. 2022 г.

Reviewer:

Prof. Dr. Vanya Gerova – Nankova, PhD

