

ACADEMIC REVIEW

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Subject: PhD-thesis for the award of an **educational and scientific degree "PhD"**

to Dr. Veselin Rosenov Chonov

PhD-thesis topic: "**EXPRESSION OF EPITHELIAL AND MESENCHYMAL
MARKERS, Ki-67, Twist AND Snail IN THE PROGRESSION AND METASTASIS OF
GASTRIC CARCINOMA**"

Scientific supervisor:

Prof. Dr. Elena Galabova Poryazova-Markova, MD, PhD

Brief biographical data

Dr. Veselin Rosenov Chonov was born on 5.03.1988 in Plovdiv. In 2007 he graduated from the Language School - Plovdiv with a German language profile. He started to study "Medicine" at MU-Plovdiv, where in 2013 he graduated as a doctor, and from the same year he began his work experience and specialization at the Department of General and Clinical Pathology of the Medical University - Plovdiv and UMHAT "Kaspela". In 2018 he acquired a specialty in "General and Clinical Pathology", and a year later he joined the Department as an assistant professor. Since 2023 he has been a PhD-student independently preparing the topic of the PhD-thesis "Expression of epithelial and mesenchymal markers, Ki-67, TWIST and SNAIL in the progression and metastasis of gastric carcinoma" with scientific supervisor Prof. Dr. Elena Galabova Poryazova-Markova, MD, PhD. Dr. Chonov is fluent in English and German, and he is a member of the Bulgarian Medical Union, the Bulgarian Society of Pathology, and the European Society of Pathology.

Relevance of the topic and characteristics of the dissertation work

The PhD work of Dr. Veselin Rosenov Chonov is written on a total of 174 pages and includes the following parts: Introduction, Literature review, Aim and objectives, Material and methods, Own results, Discussion, Findings and Conclusion, Contributions, Publications and participation in scientific congresses related to the PhD work, Bibliography.

At the beginning, Dr. Chonov presents the abbreviations used in the text. This is followed by a short “**Introduction**” within three pages, which presents brief data on the spread of gastric cancer (GC), the etiopathogenetic factors in its development, and the classification. Emphasis is placed on the role of epithelial-mesenchymal transition (EMT), comparing the expression of individual biomarkers in the development of tumor processes.

The following is the chapter “**Literature Review**”, which includes ten subchapters, in which the author consistently and synthesized describes the information available in the literature regarding: the definition and epidemiology of GC, presenting modern data based on GLOBOCAN 2020, as well as the relationship with some etiological factors. This is followed by a description of the etiopathogenetic factors in the development of the neoplasm, with emphasis on the role of *Helicobacter pylori*, *Epstein-Barr* virus, genetic and hereditary risk factors, including factors related to family syndromes, as well as environmental factors. In the subchapters related to the diagnosis, therapy and classification of the disease, modern approaches and directions in oncology are presented, with a particularly thorough description of the morphological classifications and the associated alterations in the GC structure, the relationship with the prognosis and prediction of the disease. Significant emphasis is placed on the conceptual profile underlying the foundations of the dissertation work, namely - the epithelial-mesenchymal transition and the molecules associated with it. The role of EMF in various carcinomas and in particular SC is discussed, as well as its importance for the invasion, plasticity, migration and malignant transformation of cells. The role and participation of the markers: E-cadherin, vimentin, SNAIL and TWIST, as well as the proliferative marker Ki-67, and their relationship with the process - the subject of the study in the work, are presented. At the end of the chapter, a brief analysis is made and conclusions from the review are formulated.

In the next chapter “**Aim and objectives**” Dr. Chonov formulates the aim of his study, namely – to investigate the immunohistochemical expression of the epithelial marker E-cadherin, the mesenchymal marker Vimentin, the transcription factors Snail and Twist, and the proliferative marker Ki – 67 in patients with gastric cancer and their relationship with the clinical and morphological characteristics of the tumor in order to clarify their role in tumor progression. To achieve this aim, a total of five objectives are presented – directly related to the aim, and it is expected that a number of morphological, immunohistochemical and comparative analyses with the available clinical and morphological data will be carried out.

In the chapter “**Material and methods**” it is visible that the study includes a retrospective and prospective study of 158 cases with histologically diagnosed gastric cancer for a period of seven years, both endoscopic and resection materials. The histological types of

carcinomas are described, as well as groups of carcinomas and lymph node metastases are distributed. The methods present the classical histological technique, the immunohistochemical study including the five monoclonals - E-cadherin, vimentin, SNAIL and TWIST, as well as Ki-67, the components for performing the study, as well as the relevant protocols for reporting each of the markers. At the end of the chapter, the statistical methods of research are presented, taking into account the specifics of the tasks set and the type of variables studied.

The section "**Own results**" is organized in the order of presentation of the tasks and their subtasks, commented on in the previous section of the PhD-work. Task 1 compared gender and age differences in patients with intestinal and diffuse type of gastric cancer, described the characteristics based on over and under 45 years, the distribution by decades, distribution based on histological classification, grading, tumor and nodal status, as well as invasion into vessels and perineural invasion. Within the framework of task 2, an IHC study with E-cadherin, Snail, Twist and Vimentin and their relationship with clinicomorphological indicators is presented, and for each of the markers, tabular, graphic and photographic material demonstrating expression, degree and relationship with the indicators is presented, and statistically significant differences are sought. The third task demonstrated particularly interesting results, as within its framework the correlation between the immunohistochemical expression of the markers associated with the epithelial-mesenchymal transition – E-cadherin, Snail, Twist and Vimentin in the group with metastatic gastric carcinoma in lymph nodes and the relationship with individual clinical and morphological indicators was sought. In task 4, which analyzed the relationship between the immunohistochemical expression of the markers of the epithelial-mesenchymal transition – E-cadherin, Snail, Twist and Vimentin in the groups with primary tumor and lymph node metastases from GC, the expression in both locations was studied in depth, and although a statistically significant result was found only in relation to the expression of Vimentin, as well as a trend in relation to the expression of E-cadherin, the results are demonstrative and interesting. In the next task 5, the results of the study of the expression of the proliferative marker Ki-67 in the groups with primary tumor and lymph node metastases from gastric cancer are demonstrated and the relationship with the individual clinical and morphological indicators is assessed, and some significant and trending conclusions are again outlined, supporting evidence of part of the hypotheses set out in the study, with a subdivision being made in separate paragraphs.

In the chapter "**Discussion**", the results of the tasks are again presented in a summary, with the emphasis placed on the significant ones, as well as those in which a clear trend is outlined. All findings are discussed and summarized by Dr. Chonov, and the scientific literature of other authors available to the PhD-thesis is searched and compared. The contemporary comparative approach is clearly visible, as is the attempt to search for and find an explanation for the obtained own findings.

The presented "**Findings**" are 13 in number, the first six of which are related to the correlation between clinical and some demographic parameters and the classification and morphological finding in the cases. The next seven are based on significant results of the study and are directly related to the sources discovered by the PhD-student, correlating the tasks added at the beginning of the dissertation. In addition, six "**Conclusions**" are presented.

The "**Contributions**" are divided into those of an original nature - a total of five, as well as those of a responsible nature - again five in number.

Dr. Veselin Chonov presents three **publications** related to the topic of the PhD-thesis, one of which is the first author, as well as five **participations** in scientific forums.

The bibliography contains 271 titles, 3 of which are in Bulgarian or in bulgarian editions and 269 in latin, most of which are referenced and indexed in world databases.

The entire work is illustrated with 41 figures, 64 tables, and 22 microphotographs.

In addition – the presented abstract is a synthesized material, including the most important text elements, tables, graphs and photos from the dissertation work.

Critical notes and suggestions


Similar ones were made by me in previous moments of the procedure, and I find that most of them have been fulfilled. I could recommend most of the results of the obtained studies in a significant group of patients and materials to be published in highly referenced and indexed scientific studies.

Conclusion

In conclusion, the PhD work thus submitted for evaluation for the award of the ESD "PhD" is an extensive, interesting and fully completed scientific work, which includes all mandatory elements, results, conclusions and contributions made based on them. The same could be continued, deepened and expanded in the next stage of research, as the information in the work could be of assistance to many basic and clinical specialists in their scientific research.

Based on this, I convincingly give my **positive assessment and vote "YES"** the award of the ESD "PhD" to **Dr. Vesselin Rosenov Chonov**, in the PhD program "Pathoanatomy and Cytopathology", field of higher education 7. Health and Sports, professional field 7.1 Medicine, and I recommended on the other members of the esteemed jury to support the candidate with a positive vote.

10/08/2025


Prof. Dr. Julian Rumenov Ananiev, MD, PhD

Заличено на основание
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