

STATEMENT

by Assoc. Prof. Jeli azko Iliev Arabadjiev, MD, PhD

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According to the Order of the Rector of MU Varna № R-109-567/19.12.2023 I have been elected as a member of the Scientific Jury in the procedure for the acquisition of the educational and scientific degree "Doctor" in the scientific specialty "Oncology" of the PhD student in full-time training - Dr. Maria Ivanova Penkova-Ivanova with the topic of her dissertation: "Expression of tumor reversion markers in colorectal cancer". Scientific supervisor of the dissertation is Assoc. Prof. Eleonora Georgieva Dimitrova-Gospodinova, PhD.

Brief biography of the dissertant:

Dr. Maria Ivanova Penkova-Ivanova graduated from secondary education at Dobri Chintulov Natural and Mathematical High School – Sliven with a degree in Biology, Chemistry and German. In 2016 she graduated with excellent grades in medicine from Medical University "Prof. Dr. Paraskev Stoyanov" - Varna. Since 2018 she has been appointed as a resident at the Clinic of Medical Oncology of the University Hospital "St. Marina" - Varna and as a regular assistant at the Department of Propaedeutics Internal Medicine of Medical University - Varna, English-speaking training. Since 2020 she has been reassigned to the newly formed Department of Oncology, where she is also enrolled as a regular PhD student after successfully passing the competitive examination. Dr. Maria Penkova-Ivanova is fluent in English and German. She is a member of the European Society of Medical Oncology (ESMO).

Theme, content and introduction of the dissertation

Globally, colorectal cancer (CRC) ranks third among human malignancies and accounts for approximately 11% of all malignant solid tumors. GLOBOCAN 2020 data show that the number of new cases worldwide reaches 2 million annually. CRC is the second most common cause of death from malignancy, with almost 1 million deaths recorded in 2020, despite the availability of effective screening methods and advanced treatment techniques. Early detection and treatment of CRC helps to prolong survival and improve the quality of life of patients. The search for new

markers (diagnostic and prognostic) that can aid this process has become increasingly relevant in recent years.

TCTP is a protein that, in addition to being involved in the regulation of many fundamental cellular functions, has been shown to be important in both the early stages of carcinogenesis and tumor progression. Due to its important role also in the process of tumor reversion, the interest in TCTP is nowadays significantly increasing due to its potential to be used not only as a good prognostic marker but also as a target in the treatment of malignant solid tumors. Worldwide, studies reporting the association between TCTP expression levels and overall survival in different types of malignant solid tumors are still limited. In this aspect, the proposed topic of Dr. Penkova's thesis is interesting, relevant and original. The content and the introduction are well structured with a clear graphical view, chronologically arranged and giving an insight into the object of research.

Structure and graphic design of the dissertation

The dissertation of Dr. Maria Penkova contains 117 pages and is presented graphically in 18 tables and 17 figures. The scientific work contains the following structure:

- "Introduction" - 2 pp.
- "Literary Review" - 58 pp.
- "Aim and objectives of the study" - 1 p.
- "Patient population and study methods" - 11 pp.
- "Results" - 12 pp.
- "Discussion" - 4 pp.
- "Conclusion" - 1 p.
- "Contributions" - 1 p.
- "Contributions of the scientific work" - 1 p.
- "Scientific publications and announcements related to the dissertation" - 2 pp.

The bibliography contains 274 titles, of which 1 in Cyrillic and 273 in Latin. The number of scientific publications related to the topic of the thesis is 5, 3 of which are published in international journals.

The structure of the dissertation is well organized, following the rules of volume between the different sections and directly corresponding to the requirements of the Law for the Development of Scientific Staff of the Republic of Bulgaria.

Review of the scientific literature in relation to the object of the research

Dr. Penkova presents a detailed literature review of an extensive volume of scientific publications covering up-to-date information on the epidemiology, etiology, pathogenesis of this oncological disease, as well as on the currently applied in clinical practice diagnostic, predictive and prognostic genetic and epigenetic biomarkers in CRC, as well as the most current treatment strategies. The last two parts of the literature review discuss in detail the role, relationship and impact of TCTP expression levels on carcinogenesis and tumor reversion. The results of studies conducted worldwide to date are presented in tables, as the number of studies of this type in the European population is scarce and none have been conducted in the Bulgarian population.

Materials and specific research methods

In the framework of the study, the dissertator selected 74 patients with histologically verified CRC who met predefined criteria. The steps for preparation and immunohistochemical examination of biopsy materials are described in detail, as well as the methods for reporting TCTP expression levels. The methods used for statistical and descriptive processing of the obtained results are presented chronologically.

Aim, Objectives, Results, Conclusions and Contributions of the Dissertation

The aim and objectives are clearly defined. The results obtained are well analyzed in the discussion and summarized in the conclusions and contributions of the scientific work. The available figures, graphs and tables facilitate and support the successful understanding of the researched topic. Of the results obtained, the following can be highlighted as more significant:

- Higher nuclear levels of TCTP expression in primary tumor cells in patients with histologically verified CRC are associated with the presence of a greater number of metastatic foci in stage IV patients and a higher degree of tumor differentiation.
- Higher nuclear levels of TCTP expression in primary tumor cells in patients with histologically verified CRC are associated with shorter progression-free survival and shorter overall survival
- High nuclear TCTP levels are an independent prognostic factor for worse progression-free survival and overall survival.

Scientific publications related to the topic of the thesis are 5 in number, 3 of which are published in international journals.

The abstract consists of 52 pages and the main chapters of the thesis are presented chronologically.

Conclusion

The dissertation work of Dr. Maria Penkova-Ivanova represents a thorough and significant scientific research in the field of clinical oncology. The study is modern and scientifically substantiated by the applied methods. The scientific work of Dr. Penkova fully complies with all the requirements of the Academic Staff Development Act of the Republic of Bulgaria.

On the basis of the above I give a positive evaluation of the dissertation work of Dr. Maria Ivanova Penkova-Ivanova and propose to the members of the esteemed Scientific Jury to award her educational and scientific degree “DOCTOR”.

Sincerely

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/Assoc prof. Jelialzko Arabadjiev, MD, PhD/