

Short Academic Review

From **Assoc. Prof. Julian Rumenov Ananiev, MD, PhD**

Dean of Medical Faculty, Trakia University,

Associate Professor in the Department of General and Clinical Pathology, Forensic Medicine and Deontology, and Dermatovenereology

on the PhD Thesis of: **Lilyana Nikolova Petkova, MD**

Department of "General and Clinical pathology, Forensic Medicine and Deontology" – MU – Varna, Faculty of Medicine, for acquisition of educational and scientific degree of „PhD“ in the field of higher education 7. „Health and Sport“, professional field 7.1 „Medicine“, scientific speciality „Pathoanatomy and cytopathology“,

Title: „EXPRESSION OF CYCLIN D1, BCL2, p53 AND OTHER MELANOCYTE MARKERS IN MALIGNANT SKIN MELANOMAS AND MELANOCYTE NEVI - COMPARATIVE ANALYSIS OF IMMUNOHISTOCHEMICAL EXPRESSION, MORPHOLOGICAL PROFILE, AND RELEVANCE TO DIAGNOSIS AND TUMOUR PROGRESSION“

Scientific Leader: Professor Bogomila G. Manevska, MD, MSc

The presented PhD-thesis of Lilyana Nikolova Petkova, MD is written on a total of 148 pages and includes parts: introduction, review, aims and objectives, material and methods, results, discussion, conclusions, contributions, references. In addition to the invariable part of these materials is the short review, in a total of 108 pages, which are presented the main part of the thesis, the publications related to the thesis and participation in scientific forums.

The thesis begins with a chapter "Introduction", in which Dr. Petkova emphasizes the debatable issues related to melanomas, their progression and morphological methods and markers used in the study.

Following is the chapter "Review", in which a total of 42 pages, the author thoroughly and gradually presents the prevalence of pigmented tumors, etiology and pathogenesis in their development. The following is a synthetic analysis of the classification of melanocytic lesions, describing most of the known types and using the latest WHO classification. A separate subchapter describes the methods used in routine diagnosis, as well as specific immunohistochemical markers, as well as markers related to tumor genesis and biological behavior of tumors, in particular important for pigmented tumors. The chapter ends with a brief conclusion and a reference to the main problems that Dr. Petkova outlines for consideration and resolution in the following chapters.

In the chapter "Aims and Objectives" Dr. Petkova aims to select a cohort of benign and malignant pigmented skin tumors, to perform immunohistochemical analysis of the expression of some melanocytes (S100 protein, Melanosome clone HMB45) and non-melanocytes (Cyclin D1, BCL2, p53 protein) markers in order to look for significant differences that allow the development of criteria to support morphological diagnosis, especially for the differentiation of borderline lesions and malignant melanoma, and for possible prediction of biological behavior in these tumors. Five objectives are described in detail in direct relation to the set goal.

Next chapter is "Materials and Methods", where Dr. Petkova collects and analyzes material from a total of 5 years. 91 pigmented neoplasms are presented as follows: 57 benign melanocyte nevi, 10 atypical nevi and 24 malignant melanomas (MM) accompanied by clinical history of biopsy protocols. A permit issued by the Ethics Commission with number 91 / 27.02.2020 has been declared. The following is a description of the methods, including: macroscopic analysis and section of the examined material, description of the histological processing of the materials, as well as a detailed description of the IHC protocol, components and evaluation of the results. In a separate subchapter, the author describes the applied statistical methods and statistical software.

The chapter "Results" is the most extensive and detailed structured chapter, in which the PhD-student presents the results and analyzes of the following: demographic indicators and correlations; the topographic distribution of melanocyte lesions; the main morphological characteristics of the studied material by groups; data from the expression results of Cyclin D1, BCL2, p53, S100, HMB 45 and Ki67. In addition, at the end of the chapter, the study on the immunoreactivity of all markers in the three groups of pigment tumors demonstrated differences

in expression between the groups, based on additional studies of statistical significance as predictors of malignant potential in two design protocols.

In the chapter "Discussion", Dr. Petkova analyzes the data from the previous chapter and comparing them with the data that she found in the literature, makes a successful attempt to explain and discuss its results. Based on contemporary publications, the author brings out the similarities and differences, fully responding to the necessary analysis-synthesis of the results achieved, and the discussion follows each result obtained, comparing the data in the literature with the result of the dissertation.

In the chapter "Conclusion" Dr. Petkova summarizes the previous results and based on their basis, confirms the need for the application of the studied markers, deriving the conclusions presented in the next chapter.

The thesis concludes with the chapters "Conclusions" and "Contributions", in which Dr. Petkova presents twelve conclusions, two original scientific and applied contributions and four confirmatory contributions.

The dissertation contains 41 figures and 30 tables. The references includes a total of 126 literature sources, of which 10 in Cyrillic and 116 in Latin.

Dr. Petkova presents four full-text publications and three forum attendances.

Based on the above, I believe that the PhD Thesis of Lilyana Nikolova Petkova, MD is a **fully completed scientific study with scientifically applicable and diagnostically significant contributions.**

I confidently give my positive assessment and I will vote "Positive" for acquisition of educational and scientific „PhD“ degree to Lilyana Nikolova Petkova, MD in the field of higher education 7. "Health and Sports", professional field 7.1 "Medicine", scientific specialty "Pathology and Cytopathology ", and I also recommend the honorable members of the scientific jury to support this choice as well.



Stara Zagora
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Assoc. Prof. Julian Rumenov Ananiev, MD, PhD