

ACADEMIC REVIEW

by Assoc. Prof. Dr. EKATERINA BOYANOVA SOFTOVA-ZLATAROVA, MD, PhD

Specialty Pathology and Cytopathology, MC "City Lab" Ltd.

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

„PhD”

To Dr. PLAMEN PETROV VASSILEV

PhD-thesis topic: **"APOPTOSIS AND NECROPTOSIS IN BASAL CELL AND
SPINOCELLULAR SKIN CARCINOMA"**

Professional direction: 7.1. Medicine

PhD program "Pathologic anatomy and cytopathology"

Scientific supervisor: Prof. Dr. Maria Angelova Tsaneva, MD, PhD

By Order № P-109-427/06.10.2025 of the Rector of MU-Varna, Prof. Dr. Dimitar Raykov, MD, DMSc, in view of report ext. № 102/2240/19.09.2025 by Assoc. Prof. Dr. Deyan Lyudmilov Dzhenukov, MD, PhD, Head of the Department of General and Clinical Pathology, Forensic Medicine and Deontology, by decision under Protocol № 46/29.09.2025 of the Faculty of Medicine, and report ext. № 103/6377/30.09.2025 by Prof. Dr. Yoto Trifonov Yotov, MD, PhD, Dean of the Faculty of Medicine, and on the basis of Art. 24(6) and Art. 30(3) of the PPZRASRB, and Art. 68(1) of the Rules for the Development of Academic Staff at MU-Varna, Dr. Plamen Petrov Vassilev, PhD student enrolled full-time in the doctoral program "Pathology and Cytopathology", professional field 7.1 "Medicine", admitted by Order № R-109-488/04.11.2020, has completed the program with the right to defend his dissertation. According to Order № R-109-427/06.10.2025 of the Rector of MU-Varna, I was appointed as an external member of the scientific jury, and on the basis of Protocol № 1/14.10.2025, I have been tasked with preparing an academic review in the procedure for awarding the educational and scientific degree of "Doctor" to Dr. Plamen Petrov Vassilev.

The PhD student has submitted both paper and electronic copies of the required documents in accordance with the requirements of the ZRASRB, its implementing regulations, and the Rules of Procedure at MU-Varna, including the dissertation, abstract, biographical data, administrative documents, the protocol dated 25.02.2022 for the successfully passed doctoral minimum exam (overall grade: Very Good 5.34), and the protocol of the foreign language exam dated 20.05.2021 (result: Passed).

Short details of the PhD student

Dr. Plamen Petrov Vassilev was born on 13.10.1974 in the city of Burgas and studied and completed his secondary education from 1989 to 1992. In 1994, Dr. Vassilev was admitted as a student at the Medical University of Sofia, where he graduated in 2000 with a Master's degree in Medicine. He obtained professional qualification as Master – Doctor, MU Sofia, MYC series No. 009778, registration No. 6918/13.11.2000. After successfully passing the State Exam, as of January 1, 2011, Dr. Vassilev acquired the rights of a specialist in Clinical Laboratory (certificate of recognized specialty, reg. No. 015832/31.01.2011, series MYB–2011, No. 3038). By Protocol No. 4 of 05.03.2015, he acquired a professional qualification in the specialty of Health Management (certificate of recognized specialty, reg. No. 2015009/16.03.2015, series C 2005). He successfully completed a training course in Medical Pedagogy (certificate, reg. No. 3559/17.10.2016). From 2013 to 2017, Dr. Vassilev was a resident in General and Clinical Pathology at the University Hospital "St. Marina" - Varna. As of January 1, 2019, after successfully passing the State Exam, Dr. Vassilev acquired the rights of a specialist in General and Clinical Pathology (certificate of recognized specialty, reg. No. 022569/01.03.2019, MUV series 2019, No. 4091).

As a PhD and postgraduate student, Dr. Vassilev actively participates in the activities of the Clinic and the Department of Pathology at the Medical University and University Hospital "St. Marina" - Varna. The scientific interests of the PhD student are primarily focused on dermatopathology, including malignant and non-melanoma skin neoplasms, neuroendocrine pathology, thyroid diseases, female reproductive system pathology, intraoperative diagnostics, ovarian tumors, colorectal carcinoma, and related areas. Dr. Vassilev holds diplomas and certificates for participation in a variety of courses, seminars, and trainings (including language courses at different levels), the majority of which are in the fields of gynecological pathology, thyroid pathology, and breast tumors, among others. From 2005 to 2010, Dr. Vassilev was a resident at the Medical University "Prof. Dr. Paraskev Stoyanov" in Varna and at University Hospital Burgas. After obtaining his specialty, he worked as a specialist doctor in Clinical Laboratory at Veliki Preslav Hospital – Veliki Preslav, DCC "St. Iv. Rilski" – Varna, and Medical Center "St. Stiliyan" – Varna. From 2013 to 2017, Dr. Vassilev was a resident in General and Clinical Pathology at the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna and University Hospital "St. Marina" – Varna. Between November 2021 and October 2025, he is enrolled as a full-time PhD student in the Doctoral Program in Pathological Anatomy and Cytopathology. Since October 2023, he has held the position of specialist in General and Clinical Pathology at University Hospital Burgas, with primary activities in histopathology, cytopathology, and autopsy.

Dr. Vassilev is a member of the Bulgarian Medical Association and the Bulgarian Society of Pathology. He has a good command of English in reading, writing, and conversation, and holds a certificate for a German language training course at level B1. As a PhD student, he possesses excellent technical skills and competencies and is proficient in working with computers and specialized equipment.

Actuality of the problem

According to the available literature, in a large proportion of malignant neoplasms, given their tendency for progression and metastasis, it is particularly important to determine the appropriate approach and therapeutic strategy, both for implementing adequate treatment and for monitoring patient survival. This highlights the need for further studies on the biological behavior of tumors and, consequently, the possibility of uncovering molecular mechanisms that play a key role in activating the metastatic potential of specific cancers. Despite ongoing efforts to develop new molecular markers and the availability of modern prognostic criteria that can be applied in clinical practice to estimate recurrence risk, patient survival, and guide active treatment, the tendency of tumors to metastasize remains uncertain, as its role is not universal and varies depending on the biological characteristics of the tumor or its microenvironment. To better understand tumor behavior, suitable markers are continuously sought to elucidate tumor biology.

Currently, many new molecules involved in oncogenesis are under investigation in various neoplasms, including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). Identifying markers that predict the biological behavior of these tumors could significantly improve monitoring and management strategies. The present study aims to determine the predictive and prognostic value of RIPK3 and CASP-3 expression in tumor cells of carcinomas with different characteristics and degrees of differentiation. The study is innovative, up-to-date, and has the potential to identify new therapeutic strategies and prognostic indicators during the course of the disease. Basal cell carcinoma is the most common type of skin cancer, with an incidence of approximately 2,000 cases per 100,000 people and an increasing trend in individuals over the age of 50. BCC is characterized by slow growth, rare metastasis, and a fatal outcome in less than 0.1% of patients. Regarding anatomical distribution, the highest percentage of tumors occurs on the head and neck (approximately 85%), followed by the trunk and limbs (about 15%), and least frequently in the genital area. Important etiological factors include exposure to arsenic, tar, ultraviolet and ionizing radiation, and decreased local immune status. In addition, skin color plays a significant role, as individuals with lighter skin are more susceptible to BCC. Men are approximately twice as likely to be affected as women, with a ratio of 2:1. According to literature data, BCC accounts for approximately 80% of all skin cancer cases in the United States, while SCC represents about 20%. Squamous cell carcinoma (SCC) is the second most common type of skin cancer among white individuals, with incidence typically increasing after the age of 50. It is observed 2–3 times more frequently in men, particularly around the age of 70. SCC generally exhibits slow growth and rarely metastasizes; however, in approximately 0.5% of cases, it may cause local tissue destruction. The highest incidence of cutaneous SCC has been reported in Australia. Literature data indicate that about 1 million cases are diagnosed annually in the United States.

The etiological factors contributing to squamous cell carcinoma (SCC) are largely similar to those implicated in basal cell carcinoma, including ultraviolet (UV) radiation, local immunosuppression, ionizing radiation, and exposure to chemical carcinogens such as resins, tar,

arsenic, and other industrial compounds. Infection with various types of human papillomavirus (HPV), including types 5, 8, 9, and 16, also contributes to tumor development. Individuals with fair skin (phototypes I and II), as well as those with blond or red hair, are at an increased risk of developing SCC.

In Bulgaria, malignant skin tumors are among the most common malignancies. In 2011, 4,783 new cases were diagnosed in both sexes, corresponding to approximately 13 new cases per day, with incidence increasing with age. The most affected age group is 80–84 years. Since 2000, a steady increase in both morbidity and mortality has been observed. With an annual growth rate of approximately 10%, basal cell carcinoma is expected to surpass all other malignant neoplasms in frequency.

The determination of the main histological variants of squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) is based on the 2018 WHO classification of skin tumors, revised in 2023. According to this classification, BCC variants are categorized as low-risk (superficial, nodular, infundibulocystic, fibroepithelial) and high-risk (basosquamous, BCC with sarcomatoid differentiation, infiltrative, sclerosing/morphea-type, and micronodular). Currently, similar to other tumor types, treatment decisions and prognosis in patients are determined by tumor stage, histological subtype, and degree of differentiation.

The main mechanism of chemotherapy-induced cell death is generally considered to be apoptosis. However, some cells exhibit innate or acquired resistance to pro-apoptotic stimuli. In such cases, induction of non-apoptotic cell death provides alternative pathways to eliminate apoptosis-resistant tumor cells, highlighting the importance of exploring alternative cell death mechanisms. **Apoptosis** is a form of programmed cell death activated via two main pathways: an external pathway, initiated through death receptors on the cell membrane, and an internal pathway, triggered at the mitochondrial level in response to intracellular damage. Apoptosis is mediated by the activation of cysteine proteases called caspases, with caspases 8 and 9 initiating the signaling cascade that ultimately leads to cell death, in which caspase-3 acts as a central executor. **Necroptosis** is a relatively newly characterized form of programmed cell death, also stimulated by classical death receptors, similar to the external apoptosis pathway. Necroptosis is mediated by receptor-interacting protein kinases RIPK1 and RIPK3, which form a complex known as the necrosome, leading to increased cell membrane permeability via a cascade of phosphorylation events. Unlike apoptosis, the nuclei of necroptotic cells remain intact. **Induction of necroptosis in cells with defective apoptotic pathways represents a potential therapeutic strategy.**

The structure of the dissertation complies with the requirements of the Law on the Prevention of Corruption and the Regulations of MU-Varna. It comprises 139 pages and is illustrated with 66 tables and 35 figures. The bibliography includes 355 references, of which 6 are in Cyrillic and 349 in Latin. The distribution of pages by section is as follows: title page – 1; table of contents and list of abbreviations – 4; introduction – 2; literature review – 53; objectives – 1; materials and methods – 5; results and discussion – 43; conclusions – 1; contributions – 1; bibliography – 21.

The literature review is comprehensive and up-to-date, providing a detailed analysis of the epidemiology of malignant skin neoplasms, their distribution by sex, and genetic predispositions, including nine syndromes associated with these tumors. It also examines risk factors and the current WHO classification (2017) with its 2023 update, which play a significant role in understanding the development of malignant skin neoplasms.

The aim of this study is to investigate the immunohistochemical (IHC) expression of the apoptosis marker Caspase-3 and the necroptosis marker RIPK3 in patients with basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) of the skin, and to assess their predictive value.

In line with the study aim, seven specific tasks have been formulated as follows:

1. To investigate the clinical and morphological characteristics of patients with BCC and SCC.
2. To determine the level of immunohistochemical (IHC) expression of Caspase-3 in the tumor tissue of BCC and SCC.
3. To compare the IHC expression of Caspase-3 in tumor tissue of SCC and BCC with adjacent non-tumor tissue.
4. To analyze Caspase-3 expression in relation to clinical and morphological parameters, including patient age and sex, tumor-infiltrating lymphocytes (TILs), tumor necrosis, degree of differentiation, tumor size, and localization.
5. To determine the level of IHC expression of RIPK3 in the tumor tissue of both cancers.
6. To compare the IHC expression of RIPK3 in tumor tissue of the two skin cancers with adjacent non-tumor tissue.
7. To analyze RIPK3 expression in relation to the above clinical and morphological parameters, including patient age and sex, TILs, tumor necrosis, risk group, degree of differentiation, and tumor localization.

These tasks are well justified, feasible, and fully aligned with the stated research objective.

Material and methods: The dissertation was conducted at the Department of General and Clinical Pathology, Forensic Medicine, and Deontology at MU-Varna, as well as at DCC "St. Marina," and included material from 91 patients. 1. Routine analyses were performed, including the preparation of standard histological sections. 2. Immunohistochemical (IHC) analyses were performed using an indirect immunoperoxidase method with the Mini KIT High Ph DAKO K8024. The reagents, antibodies, and working concentrations used are presented in Tables 4 and 5. The protocol for preparing biopsy materials for IHC, as well as the method for evaluating the expression of Caspase-3 and RIPK3 and the formula applied, are described in detail. Statistical analyses included descriptive statistics, the Student's t-test for two independent samples, and analysis of variance (ANOVA).

Results: The study, conducted over a period of seven years (2015–2021), included a total of 91 patients, comprising 46 with basal cell carcinoma (BCC) and 45 with squamous cell

carcinoma (SCC). The mean age of all patients was 58.3 ± 14.47 years, with 56.5 ± 13.5 years for BCC patients and 60.2 ± 15.32 years for SCC patients. Among the SCC patients, 25 were men (55.6%), while BCC was more prevalent in women, with 20 male patients (44.5%). Histological subtypes were distributed as follows: among the 46 BCC patients, 24 (52.17%) had the nodular subtype, 10 (21.74%) the superficial subtype, 7 (15.22%) fibroepithelial, and 5 (10.87%) micronodular. Of the 45 SCC patients, 33 (73.33%) presented with the conventional subtype, 5 (11.11%) with the verrucous subtype, and 7 (15.56%) with keratoacanthoma-like carcinoma. Gender distribution showed that BCC was more common in women, with a female-to-male ratio of 1.3:1, whereas SCC was more common in men, with a male-to-female ratio of 1.25:1. Regarding tumor differentiation, 30 SCC patients (66.67%) and 34 BCC patients (73.91%) were classified as grade G1, while 15 SCC patients (33.33%) and 12 BCC patients (26.09%) were classified as grade G2. Tumor staging revealed that 43 SCC patients (95.56%) were in stage T1 and 2 (4.44%) in stage T2, while all BCC cases (46 patients, 100%) were stage T1. Tumor localization analysis showed that SCC occurred in the neck in 2 cases (4.44%), in the head in 31 cases (68.89%), in the trunk in 3 cases (6.67%), on the limbs in 8 cases (17.78%), and in the genital area in 1 case (2.22%). BCC was localized in the head in 37 cases (80.43%), trunk in 4 cases (8.7%), limbs in 2 cases (4.35%), and genital area in 3 cases (6.52%). Histological examination revealed tumor necrosis in 8 SCC cases (17.78%) and 5 BCC cases (10.87%) affecting up to 10% of the tumor area, while necrosis between 10–30% was observed in 3 SCC cases (6.67%). Tumor-infiltrating lymphocytes (TILs) were assessed in all cases: absence of TILs was found in 15 SCC cases (33.33%) and 18 BCC cases (39.13%), weak expression in 16 SCC cases (34.78%) and 22 BCC cases (48.89%), and moderate expression in 8 SCC cases (17.78%) and 12 BCC cases (26.09%). A targeted assessment of lymphovascular invasion was performed; however, no evidence of invasion was found in any of the specimens.

Results of immunohistochemical studies

1. Expression of Caspase-3, a marker of apoptosis

1.1. Caspase-3 Expression in Basal cell carcinoma /BCK/

In the tumor tissue of carcinomas, the mean cytoplasmic expression of Caspase-3 was 20.20 ± 60.44 , with a range from 0 to 300. In adjacent non-tumor tissue, the mean cytoplasmic expression was 18.02 ± 37.12 , and no statistically significant difference was observed between tumor and adjacent non-tumor tissue. The nuclear expression of Caspase-3 in tumor tissue of BCC was 17.87 ± 56.74 (range 0–293). In adjacent non-tumor tissue, the mean nuclear expression was 18.27 ± 44.35 , and no statistically significant difference was detected between tumor and non-tumor tissue. Analysis of Caspase-3 expression revealed no significant association with patient sex ($p = 0.137$ for cytoplasmic and $p = 0.160$ for nuclear expression) or tumor localization. Additionally, there was no statistically significant difference in nuclear or cytoplasmic expression of Caspase-3 between high-risk (micronodular) and low-risk (nodular, superficial, and fibroepithelial) BCC subtypes ($p = 0.412$ for cytoplasmic and $p = 0.323$ for nuclear expression).

Furthermore, Caspase-3 expression showed no significant correlation with the degree of tumor-infiltrating lymphocytes (TILs) in tumor tissue ($p = 0.549$ for cytoplasmic and $p = 0.580$ for nuclear expression) or with the presence or absence of tumor necrosis ($p = 0.434$ for cytoplasmic and $p = 0.461$ for nuclear expression).

1.2. Caspase-3 Expression in Squamous Cell Carcinoma (SCC)

The mean cytoplasmic expression of Caspase-3 in SCC tumor cells was higher compared to adjacent non-tumor tissue, and this difference was statistically significant. In contrast, nuclear expression was higher in non-tumor tissue; however, no statistically significant difference was observed between tumor and non-tumor tissue ($p = 0.579$). No significant differences were found in cytoplasmic or nuclear Caspase-3 expression in SCC tumor tissue with respect to patient sex ($p = 0.167$) or tumor localization ($p = 0.126$ for cytoplasmic, $p = 0.805$ for nuclear expression). Similarly, no statistically significant differences were observed between histological subtypes (conventional, verrucous, and keratoacanthoma-like carcinoma; $p = 0.389$ for cytoplasmic, $p = 0.449$ for nuclear expression). Analysis of Caspase-3 expression in relation to tumor differentiation revealed a statistically significant association: tumors with a lower degree of differentiation exhibited higher cytoplasmic and nuclear expression compared to tumors with higher differentiation ($p = 0.007$ for cytoplasmic, $p = 0.000066$ for nuclear expression). No statistically significant correlation was found between Caspase-3 expression and tumor-infiltrating lymphocytes (TILs) ($p = 0.059$ for cytoplasmic, $p = 0.910$ for nuclear expression) or the presence of tumor necrosis ($p = 0.585$ for cytoplasmic, $p = 0.541$ for nuclear expression).

2. Expression of RIPK3, a marker of necroptosis

2.1. RIPK3 expression in basal cell carcinoma

The study found that the mean cytoplasmic expression of RIPK3 in BCC tumor tissue was 121.72 ± 98.66 , which was significantly higher than in adjacent non-tumor tissue, with a statistically significant difference ($p = 0.0007$). The mean nuclear expression of RIPK3 in tumor tissue was 117.56 ± 109.12 , higher than in non-tumor tissue (101.04 ± 77.09); however, this difference was not statistically significant ($p = 0.305$). Cytoplasmic and nuclear RIPK3 expression was higher in high-risk histological subtypes, such as the micronodular subtype, compared to low-risk subtypes (nodular, superficial, and fibroepithelial), with statistically significant differences (cytoplasmic: $p = 0.048$; nuclear: $p = 0.047$). Regarding tumor-infiltrating lymphocytes (TILs), moderately pronounced infiltration was associated with higher cytoplasmic and nuclear RIPK3 expression compared to low or absent infiltration ($p = 0.025$). In cases with tumor necrosis, mean cytoplasmic expression was 225.20 ± 78.83 and nuclear expression was 243.60 ± 68.11 , which were significantly higher than in cases without necrosis (cytoplasmic: 109.10 ± 93.95 ; nuclear: 103.41 ± 105.32 ; $p = 0.011$ and $p = 0.006$, respectively). No statistically significant differences in RIPK3 expression were observed with respect to patient sex (cytoplasmic: $p = 0.347$; nuclear: $p = 0.420$) or tumor localization (cytoplasmic: $p = 0.661$; nuclear: $p = 0.661$).

2.2. RIPK3 expression in squamous cell carcinoma

The mean cytoplasmic and nuclear expression of RIPK3 in SCC tumor tissue was higher than in adjacent, tumor-unaffected tissue, with statistically significant differences (cytoplasmic: $p = 0.000010$; nuclear: $p = 0.000055$). No statistically significant differences were observed in cytoplasmic or nuclear RIPK3 expression with respect to patient sex in adjacent, tumor-unaffected tissue (cytoplasmic: $p = 0.384$; nuclear: $p = 0.429$). No statistically significant differences were observed in cytoplasmic RIPK3 expression across different tumor localizations in SCC tumor tissue. Nuclear RIPK3 expression in SCC tumor cells localized in the head region was higher compared to tumors on the extremities, with the difference being statistically significant. No statistically significant differences were observed in cytoplasmic or nuclear RIPK3 expression among different histological types of SCC (conventional, verrucous, keratoacanthoma-like; cytoplasmic: $p = 0.103$, nuclear: $p = 0.246$). No statistically significant differences were observed in cytoplasmic or nuclear RIPK3 expression according to the degree of tumor differentiation (cytoplasmic: $p = 0.479$; nuclear: $p = 0.298$). In SCC tumor tissue, mean cytoplasmic and nuclear RIPK3 expression was higher in cases with pronounced TIL infiltration compared to low infiltration, with the differences being statistically significant (cytoplasmic: $p = 0.000068$; nuclear: $p = 0.006298$). Mean cytoplasmic RIPK3 expression in SCC tumor tissue did not significantly differ with respect to the presence or absence of necrosis ($p = 0.063$). In contrast, nuclear RIPK3 expression was higher in tumors with a larger area of necrosis, with the difference being statistically significant ($p = 0.05$).

The results of this study have significant potential for application in both scientific research and clinical practice, particularly given the importance of a correctly defined diagnostic and therapeutic approach. The use of novel prognostic markers may enable targeted therapeutic interventions. Analysis of the expression of apoptosis and necroptosis markers in relation to histological characteristics, tumor differentiation, and stage could contribute to predicting disease progression and facilitate the identification of new signaling pathways for therapeutic targeting. Elucidation of these molecular pathways would provide critical information for validating potential therapeutic targets and obtaining data necessary for prognostic assessment in patients with skin cancer.

In the "**Results and discussion**" chapter, the study's own results are examined sequentially and compared with findings from numerous authors, analyzing the similarities and differences observed in the reported data. Dr. Vassilev presents 16 well-founded conclusions in his dissertation, the most important of which are:

- Cytoplasmic and nuclear expression of Caspase-3 in BCC and SCC tumor tissue does not correlate with patient age.
- In both BCC and SCC, cytoplasmic and nuclear expression of the apoptotic protein shows no dependence on patient sex, the extent of tumor necrosis, TIL infiltration, or tumor localization.
- In SCC, cytoplasmic expression of RIPK3 in tumor tissue increases with patient age.

- In BCC, cytoplasmic and nuclear RIPK3 expression is higher in high-risk histological variants compared to low-risk variants. In SCC, RIPK3 expression shows no dependence on histological subtype for either cytoplasmic or nuclear localization.
- Moderately and poorly differentiated SCCs exhibit higher cytoplasmic and nuclear Caspase-3 expression compared to well-differentiated tumors.

The scientific results achieved and presented in this dissertation have significant theoretical and applied relevance, with original contributions related to:

1. The implementation of comprehensive clinicomorphological and immunohistochemical (IHC) analyses of apoptosis and necroptosis in patients with SCC and BCC.

2. Analysis of the obtained IHC expression data of CASP-3 and RIPK3 to clarify their relationships with clinical and morphological parameters.

The practical and applied scientific contributions, totaling eight, involve the analysis of these two markers in relation to clinical and morphological indicators, as well as their comparison and evaluation to determine prognostic value in SCC and BCC.

Scientific publications on the topic of the dissertation

Dr. Vassilev has presented two publications in connection with his dissertation:

1. Plamen Vassilev, Ilko Bakardzhiev - "Expression of markers for apoptosis and necroptosis caspase-3 and receptor-interacting protein-kinase 3 in malignant neoplasms"; Varna Medical Forum, vol.12,2023, issue 1, MU-Varna, /122-133/
2. Plamen Vassilev - "Update of the classification of squamous cell cutaneous carcinoma; MU-Varna; Varna Medical Forum, v.12, 2023; Issue 2, / 25-38/

The abstract comprises 91 pages and provides a concise yet comprehensive summary of the dissertation.

In conclusion, Dr. Plamen Petrov Vassilev's dissertation represents a comprehensive study addressing the diagnosis and prognosis of the most common malignant skin tumors, BCC and SCC. The results obtained and the conclusions drawn are of practical relevance. Further studies involving larger patient cohorts, as well as integration of genomic data, are warranted. I recommend that the distinguished members of the scientific jury vote in favor of awarding Dr. Plamen Vassilev the degree of "DOCTOR" in the scientific specialty of "Pathological Anatomy and Cytopathology."

18.11.2025
Varna

Assoc. Prof. D

Заличено на основание чл. 5, §1, б. „Б“ от Регламент (ЕС) 2016/679
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