

STATEMENT

by Assoc. Prof. Strahil Asenov Strashilov, M.D, Ph.D., Faculty of Health Care, Department of Nursing Surgical Care, Medical University – Pleven, Pleven, Bulgaria.

Regarding the dissertation of Georgi Dimitrov Blazhev, a Ph.D. student at the Department of Genetics, Faculty of Biology, Sofia University "St. Kliment Ohridski" on the topic: "Multi-omics approach for analyzing the biological and clinical heterogeneity of some rare malignant diseases" with scientific supervisor Assoc. Prof. Velizar Stefanov Shivarov, M.D., for awarding the educational and scientific degree "Doctor", doctoral program "Genetics", professional field 4.3. Biological Sciences, area of higher education 4. Natural Sciences, Mathematics, and Informatics.

1. General information

The set of materials presented to me, including the main dissertation text and its accompanying synopsis, is in accordance with the Rules for the Development of the Academic Staff of Sofia University "St. Kliment Ohridski". In connection with the dissertation, 2 scientific articles have been published in impact factor journals. The obtained data were presented via a report at 1 national conference, thereby fulfilling the minimum requirements as per the ZRASRB.

The dissertation is typeset on 110 pages and is illustrated with 38 figures and 8 tables. A total of 173 reference sources were used. It includes the following sections: introduction – 4 pages; literature review with 15 subsections corresponding to the objectives and tasks – 26 pages; objectives and tasks – 2 pages; materials and methods – 8 pages; results – 32 pages; discussion – 8 pages; conclusion, findings, and contributions – 4 pages; appendices – 5 pages. The provided synopsis of the main text accurately reflects the content of the main dissertation work.

2. Evaluation of the Relevance of the Research Problem

Currently, malignant diseases are one of the leading causes of mortality worldwide, with Eastern Europe, including Bulgaria, having one of the highest rates. Approximately 25% of newly diagnosed cases are classified as rare types of cancer. These present a serious health and social issue due to limited expert data, a small number of patients, and a lack of sufficient clinical studies. Survival rates for these cancers vary significantly, with mesotheliomas having one of the lowest survival rates in the group. Malignant pleural mesothelioma accounts for approximately 80% of all newly diagnosed mesotheliomas. Omics technologies, including next-generation sequencing, proteomics, metabolomics, and other high-resolution techniques, are becoming established as routine methods in biomedical cancer research. Due to the generation of a large volume of diverse data by these technologies, the development of an integrative approach for analysis is necessary. In this regard, the topic of Georgi Dimitrov Blazhev's dissertation is extremely relevant and of interest to specialists in genetics and cancer biology.

3. Evaluation of Knowledge of the Research Problem

The literature review includes several sections that correspond to the objectives of the dissertation. Contemporary data on the epidemiology of malignant pleural mesothelioma, etiological factors related to its development, particularly the role of asbestos exposure, mechanisms for inducing carcinogenesis, the role of the inflammatory microenvironment, as well as the genetic aspects of this disease are presented. The next section discusses omics technologies and their application in cancer biology, justifying the need for developing integrated approaches for data analysis. The literature review demonstrates good knowledge, critical analysis, logical unification of scientific facts, and justifies the need for further research. In this regard, the aim of the dissertation is clearly and precisely formulated, namely "validation of a new prognostic score based on gene expression in patients with malignant pleural mesothelioma." To achieve this aim, nine research tasks have been skillfully determined and precisely executed by the doctoral candidate.

4. Evaluation of the Results and Contributions of the Dissertation

The results are comprehensively and accurately described. They are critically discussed in light of the most recent, similar studies. This section is well-illustrated with tables and figures. The results can be summarized in several directions:

- Integration of various omics technologies in MPM with a focus on transcriptome analysis platforms.
- A prognostic score based on gene expression in malignant pleural mesothelioma has been developed through the initial selection of genes whose expression likely affects the survival of the cell population in this disease.
- The prognostic value of the expression of the *GOLT1B* gene has been demonstrated and subsequently discussed, and the prognostic value of the expression of *MAD2L1* has been confirmed.
- An oligogenic prognostic model for MPM, including only two genes, has been demonstrated.
- The correlation of prognostic scores in MPM with certain key characteristics of this type of malignant disease, particularly those related to DNA repair and mitosis, has been clarified.
- A prognostic model with predictive value for the response to treatment with various conventional chemotherapeutic agents has been developed.

I would like to note that the obtained results, which reflect the doctoral candidate's personal contributions, are skillfully and thoroughly analyzed in accordance with the most up-to-date literature.

5. Evaluation of Contributions

The scientific contributions formulated by the doctoral candidate are clear, precise, and original, reflecting his in-depth knowledge.

6. Conclusion

In conclusion, the dissertation submitted for my opinion by Georgi Dimitrov Blazhev examines the most advanced technologies with significant potential in modern personalized medicine. I believe that the doctoral candidate has acquired theoretical, methodological knowledge and professional skills, having completed the planned tasks accurately, clearly, and in a logical sequence. I consider that the dissertation in terms of volume, content, and relevance meets the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria, and I give a positive opinion for awarding the educational and scientific degree "Doctor" in the scientific specialty "Genetics" from professional field 4.3 "Biological Sciences" to the doctoral candidate Georgi Dimitrov Blazhev.

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