



TO the Chairman of the Scientific Jury, appointed at the First Meeting of the Scientific Jury of 25.03.2025 on the basis of Order No. **R-109-148/13.03.2025** of the Rector of the Medical University of Varna

REVIEW

SUBJECT: Dissertation for the acquisition of the educational and scientific degree "Doctor" by Dr. Svilena Angelova Atanasova, doctoral student at the Second Department of Internal Medicine, Hematology Training Sector, Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" - Varna, on the topic *"Role of selected plasma microRNAs as diagnostic and prognostic markers in myelodysplastic syndrome"* in the field of higher education 7. Health and Sports, professional field 7.1. Medicine and **doctoral program "Hematology and Blood Transfusion"**, with scientific supervisor Prof. Dr. Iliana Dimitrova Micheva, MD, - Head of the Hematology Training Sector at the Second Department of Internal Medicine, Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" - Varna.

PREPARED BY REVIEW: Assoc. Prof. Trifon Georgiev Chervenkov, MD, PhD, Associate Professor of Clinical Immunology, Head of the Department of Medical Genetics, Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" - Varna, *Member of the Scientific Jury* according to Order No. **R-109-148/13.03.2025** of the Rector of the Medical University - Varna and appointed as *Chairman, internal member of the Scientific Jury, preparing a review* according to Protocol No. 1 of 25.03.2025 of the First Absentee Meeting of the Scientific Jury.

I. General data about the dissertation work of Dr. Svilena Angelova Atanasova.

The dissertation is presented in a volume of 176 pages and contains the following sections: introduction, comprehensive literature review, aim and objectives of the study, materials and methods, results, discussion, conclusion, contributions and a list of used literature. The data are visualized in 29 tables and 19 figures, with the bibliography covering 290 titles. The structure of the dissertation is logical, clear and allows for consistent tracking of the research process.



II. Assessment of the relevance of the topic

Myelodysplastic syndrome (MDS) is a complex hematological disease characterized by high heterogeneity in clinical presentation and prognosis. Modern diagnostic criteria, although well defined, often prove insufficient for precise diagnosis and prognostic assessment of patients. In this context, the need to identify new, reliable and minimally invasive biomarkers is of utmost importance. This is where the role of microRNAs as potential biomarkers appears. Therefore, the topic of the dissertation is not only extremely relevant, but also of significant practical interest.

III. Evaluation of the literature review

The literature review is developed in a thorough, comprehensive and systematic manner, providing a detailed and critical assessment of the existing scientific knowledge on myelodysplastic syndrome, its diagnosis, classification and risk stratification, as well as the epigenetic mechanisms associated with its pathogenesis. Particular attention is paid to the biological role and diagnostic and prognostic significance of microRNAs. The literature review covers all important aspects, and the literature sources used are contemporary and relevant.

IV. Evaluation of the set goals and objectives

The aim of the dissertation is clearly formulated, with the main focus being on the identification and validation of the diagnostic and prognostic value of specific plasma microRNAs in patients with MDS. The formulated tasks are precise and comprehensive, clearly defining the necessary steps to achieve the goals of the study. They include both the analysis of microRNA levels and the comparison of the obtained results with various clinical and laboratory parameters of the disease.



V. Assessment of the contingent and methods used

The study is based on a solid methodological foundation. A sufficient number of patients and an appropriately selected control group were included, which guarantees the statistical reliability of the results obtained. The subjects studied are well described, including clear inclusion and exclusion criteria. The methods applied for the analysis of microRNAs (RT- qPCR) and the statistical processing of the data (including LASSO regression analysis and Cox proportional analysis) are modern and well-founded. The author has paid special attention to the detailed description of the methodology, which allows the reproduction of the results.

VI. Evaluation of the presented results and discussion

The results are presented in clearly structured and detailed sections, accompanied by relevant tables and figures. The author makes a thorough analysis of the results and identifies specific microRNAs with potential for practical application as diagnostic and prognostic markers in MDS. The discussion is in-depth, with critical comparison of the results with data from other studies and is effective in emphasizing the novelty and significance of the achieved results.

VII. Evaluation of the contributions of the dissertation

The scientific contributions of the work are significant and original. Of particular importance is the identification of plasma microRNAs miR-144, miR-16, let-7a and miR-451a as promising biomarkers for the diagnosis and prognosis of MDS. A diagnostic model based on LASSO regression and the combination of several microRNAs (miR-22 and miR-451a) was developed, which showed extremely high sensitivity and specificity in distinguishing patients with MDS from healthy controls. These findings have the potential to optimize the diagnostic process and improve the prognostic assessment of patients, contributing to the development of personalized therapeutic approaches in hematology.



Conclusion

The dissertation work of Dr. Svilena Angelova Atanasova examines a current and scientifically significant topic with important practical applications. In my opinion, this is a stable scientific work and meets the requirements of the ZRAS of the Republic of Bulgaria and the RAS Regulations of the Medical University - Varna for the acquisition of the ONS "Doctor" and I give my positive assessment for awarding the scientific and educational degree "Doctor" in the field of higher education 7. "Healthcare and Sports", professional direction 7.1. Medicine in the scientific specialty "Hematology and Blood Transfusion" to Dr. Svilena Angelova Atanasova.

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/ Assoc. Dr. Trifon Chervenkov, Ph.D./