# OPINION

**From: Prof. Dr. Branimir Vladimirov Spassov, PhD**, MHAT "Heart and brain", Pleven

**Member of the scientific jury according to Order** P-109-82 from 21.03.2024.

**Regarding: Dissertation work for awarding the educational and scientific degree "Doctor"** in Field of higher education 4. Natural studies, mathematics and informatics, Professional direction 4.3 Biological sciences", Scientific specialty "Genetics

**Author**: Dr. Dinnar Ali Yahya, full-time assistant professor at the Department of Medical Genetics, Faculty of Medicine, Medical University – Varna

**Form of doctoral studies:** full-time

**Dissertation topic:** „Analysis of molecular-genetic markers in patients with acute myelogenous leukemia"

**Research supervisors:** Prof. Dr. Ilina Dimitrova Micheva, PhD, Second Department of Internal Diseases, Faculty of Medicine, Medical University – Varna

Assoc. Prof. Dr. Trifon Georgiev Chervenkov, PhD, Department of Medical Genetics, Faculty of Medicine, Medical University – Varna

## I. General presentation of the procedure and the PhD student

All submitted documents (a set of materials on paper and electronic media) related to the dissertation follow the requirements of the Law on the Development of the Academic Staff of the Republic of Bulgaria (ZRASRB), the regulations for its implementation and correspond to the requirements of the procedure for the acquisition of the educational and scientific degree "Doctor" at Medical University – Varna.

PhD student Dr. Dinnar Yahya was born in 1994 in Isperih. She graduated from the 8th secondary school with the teaching of foreign languages "Alexander Pushkin" in Varna in 2011. In 2017, she graduated with honors from the Faculty of Medicine of the Medical University "Prof. Dr. Paraskev Stoyanov", Varna. In April 2019, after successfully passing a competitive exam, she was appointed as a full-time assistant at the Department of Medical Genetics, Faculty of Medicine, Medical University - Varna. At the same time, Dinnar Yahya was also appointed as a specialist doctor at the Medical Genetics Laboratory at Saint Marina Medical University, Varna. In November 2020, she was enrolled as a full-time doctoral

student at the Medical Genetics Department of the University of Varna. She continues her career as a medical specialist in the Laboratory of Medical Genetics of St. Marina UMBAL and as an assistant at the Department after acquiring a specialty in May 2023.

Dr. Yahya is fluent in written and spoken English, Russian, and Turkish. She participated in scientific forums, post-graduate trainings, and courses in the country and abroad, related to cytogenetic and molecular-genetic diagnostics, genetics of onco-hematological diseases, clinical-genetic activity, genetic counseling, etc. There are 28 publications, of which 6 are in full text.

## II. Relevance of the topic of the dissertation

The thesis presented by Dr. Dinnar Yahya for opinion examines a current health problem – the need to introduce a routine method for molecular genetic diagnosis and screening in patients with acute myelogenous leukemia (AML) in our country. Genetic markers are of fundamental importance in terms of diagnosis, prognosis, prediction of therapeutic response, and follow-up of these patients. Their place in current classifications and recommendations and for work is already confirmed. The well-known genetic heterogeneity of this disease dictates the progressive need to expand and apply the knowledge of these markers in routine practice to mediate a multidisciplinary individualized approach.

Based on the facts presented above, I believe that the dissertation topic chosen by Dr. Yahya is relevant, dissertable, and of high scientific value.

## III. Knowledge of the problem

The dissertation has a volume of 130 pages. It includes 2 appendices, 15 figures, 12 tables and 201 literary sources (5 in Cyrillic and 196 in foreign languages), corresponding to the topic and correctly cited by the doctoral student. The structure of the work demonstrates a consistent and logical construction.

The good knowledge of the state of the problem is impressive - in the world and in our country, and the logical and systematic use of the cited literary material through one's own creative thought.

## IV. Dissertation work characteristics

The dissertation has a generally accepted structure and includes an introduction, literature review, research aim and objectives, patients and methods, results, discussion, conclusion,

conclusions, contributions, bibliography, list of publications and contributions, and appendices.

**The introduction** is presented clearly and concisely.

**The literature review** is of proper volume and structure, modern and informative. genetic and molecular-genetic markers' development, significance, and application, historically and today, as well as methods for their detection, are reviewed. The current classifications of the disease are also described and the role of the considered markers in them is presented.

**The set goal** is clearly defined, and the tasks logically correspond to the stages of its achievement. **Patients and methods** are clearly and sufficiently detailed described.

**The results** present the application of the molecular genetic method MLPA in newly diagnosed patients with AML over the age of 18 and the new molecular genetic markers discovered through it. The utility of this method has been demonstrated by reporting a chromosomal or monogenic finding in more than half of the included patients, and augmenting information from conventional cytogenetic analysis or compensating for a failed one in nearly a fifth of cases. Thanks to these results, patients are classified and stratified according to risk according to current work recommendations. Combining the two methods with successful definition of genetic changes in nearly 79% of patients is also commented.

**The discussion** presents a critical analysis of the success rates and limitations of the methods and their combination applied for the first time in the country to this patient population. A detailed comparison with similar studies in the country and around the world is presented.

As a result of the literature review, the own studies, and their discussion, guidelines were created to improve the work of the genetic evaluation of the contingent of newly diagnosed patients with acute myelogenous leukemia, and practical perspectives for future work were described. Also presented are 6 conclusions and 7 contributions, of which 2 - original, 3 - confirmatory and 2 - applied.

Based on the facts presented above, I consider that the goal of the dissertation work has been achieved, and the set tasks have been fulfilled.

## V. Evaluation of the publications, abstract, and the personal participation of the PhD student

The doctoral student presents 3 full-text publications on the subject, 2 of which are in a peer-reviewed foreign journal, indexed in the international databases Web of Science and Scopus. 4 scientific events were also presented - two in Bulgarian and two in international forums. She is the first author in all publications and events, unequivocally specifying her contribution to these scientific developments.

**The abstract** accurately and sufficiently reflects the most important highlights and conclusions of the research.

## VI. Conclusion

The PhD student thoroughly and systematically examines molecular genetic markers in AML and the possibility of routine molecular genetic method for genetic screening of patients in parallel with conventional cytogenetic analysis in her work. She also comments on all the factors related to the selection and application of such a method – analytical ability, technical requirements and limitations, staff training, features of the included markers, financial burden, etc., approaching this issue critically and objectively in our country.

Sufficient contributions and original proposals are available, including guidelines for improving the genetic evaluation of the newly diagnosed AML cohort. The described prospects for future work speak to the potential of Dr. Yahya's initiative for development in this field, as well as her readiness for scientific collaboration.

The dissertation meets all the requirements of the RASRB, the rules for its implementation and the rules of the MU–Varna. Based on what has been said so far, I confidently present my positive assessment of the dissertation work on the topic "Analysis of molecular genetic markers in patients with acute myelogenous leukemia" and propose to the members of the Scientific Jury to vote for awarding the educational and scientific degree "Doctor" to Dr. Dinnar Yahya.

**17.05.2024** **Prepared the statement:**.....

**/Prof. Dr. Branimir Vladimirov Spassov, PhD /**