TO: THE CHAIRMAN

TO THE SCIENTIFIC JURY

REVIEW

by **Prof. Dr. Ivanka Istalianova Dimova, MD** , Department of Medical Genetics, Medical University - Sofia, elected as a member of the Scientific Jury, determined by Order No. R-109-130 / 16 . 03 .202 6 of the Rector of the Medical University - Varna for occupying **the academic position "Associate Professor"** - 1 place, in the field of higher education 7. Healthcare and Sports, Professional Direction 7.1. Medicine, for the needs of the Department of "Medical Genetics", Faculty of Medicine of the Medical University - Varna and Laboratory of Medical Genetics at the University Hospital "St. Marina" EAD - Varna. The competition was announced in the State Gazette No. 6/16.01.2026.

Documents for participation in the competition have been submitted by one candidate – **Chief Assistant Mari Ara Hachmerian-Andreeva, MD** .

The review was prepared according to the required criteria of the Law on the Development of Academic Staff of the Republic of Bulgaria and the Regulations for its implementation, as well as the Regulations of MU-Varna for holding the academic position of "Associate Professor". The candidate's research and teaching activities were assessed based on the indicators under the Appendix to Art. 1a, para. 1 of the Regulations for the implementation of the Law on the Development of Academic Staff of the Republic of Bulgaria and according to Appendix No. 1 to the Regulations for the Development of Academic Staff at MU-Varna.

BIOGRAPHICAL DATA AND CAREER DEVELOPMENT

Dr. Mari Ara Hachmerian-Andreeva completed her higher education with a Master of Human Medicine degree in 2011 at the Medical University of Varna. In 2015, she obtained a Master of Molecular Biology and Biotechnology diploma from the Plovdiv University "Paisiy Hilendarski".

Since 2012, she has been appointed to the position of "assistant", and since 2018 - "chief assistant", in the Department of Medical Genetics of the Medical University "Prof. Dr. Paraskev Stoyanov"-Varna. Since 2018, she has been a specialist in Medical Genetics. She has two defended dissertations for the educational and scientific degree "Doctor": one in the professional field 4.3. Biological Sciences, in 2017, on the topic "Maternal biochemical screening as a method for prenatal genetic prophylaxis", and the second - in 2025 in the

professional field 7.1. Medicine on the topic "Genetic counseling in patients with probable tumor-predisposing syndrome" . Since 2019, she has been the head of the Laboratory of Medical Genetics, University Hospital "St. Marina" Varna. She is fluent in English, written and spoken.

GENERAL OVERVIEW OF SCIENTIFIC ACTIVITY

To participate in the competition, Dr. Hachmerian has submitted a total of 32 scientific papers (50% full-text publications and 50% published abstracts), of which 24 in English and 8 in Bulgarian, distributed as follows:

- **4 full-text publications in journals with impact factor**, in 1 of them (25%) she is a lead author
- **7 full-text publications in journals, refereed and indexed** in world-renowned databases for scientific information, without impact factor – in 2 of them (28%) she is the lead author
- **14 published abstracts in journals with impact factor**, in 6 of them (43%) she is a lead author
- 5 full-text publications in non-refereed journals with scientific review, in 2 of them (40%) she is the lead author
- 1 published abstract in a journal, referenced and indexed in a world-renowned database for scientific information, without impact factor
- 1 published book based on a defended dissertation for the award of the ONS "doctor" degree

The total impact factor of the presented scientific production is 4.0 for full-text publications and 58.7 for published abstracts.

Dr. Hachmerian is a member as a participant in a total of 5 scientific projects – 4 with funding from the Science Fund of MU-Varna and 1 with European funding under the Recovery and Sustainability Plan.

CHARACTERISTICS AND EVALUATION OF THE CANDIDATE

Teaching and learning activities

Dr. Hachmerian teaches "Medical Genetics" to students at the Medical University of Varna. According to the academic record for the last five years, there is an average teaching load of 241.8 teaching hours per year, including lectures (an average of 6 hours per year) and practical exercises – an average of 127.6 teaching hours per year in Bulgarian and 108.4 teaching hours per year in English.

Research activity

The main scientific contributions in Dr. Hachmerian's publications are the following:

- Development of guidelines for improving genetic counseling in patients to search for increased risk of neoplasia - in the dissertation [A1] and accompanying publications [B4.1, B4.3]
- Combined cytogenetic and iFISH approach with expanded clinical application of knowledge based on activity in oncohematology - [B4.7, B4.8, D8.26]
- Assessment of the diagnostic success rate of the applied methods for targeted panel testing with NGS technologies - [D6, D8.15]
- Optimization of algorithms for mass prenatal screening - [B4.1, D8.11]
- Socio-psychological analysis of the introduction of NIPT in Bulgaria - [B4.10, D8.20]
- Restructuring of invasive diagnostics - [B4.3, D8.27]
- Defining phenotype-genotype correlations in rare genetic syndromes with the application of facial recognition software products in the algorithm of daily practice – [G8.30, G8.6, G8.10, G8.31, G8.25].
- Transformation of genetic counseling during COVID-19 - [B4.14, D8.8]
- Assessment of understanding of genetic information - [B4.12, B4.22]

Dr. Hachmerian's extended habilitation reference covers publications 1-10, in 3 of which (30%) the candidate is the lead author. The overall impact factor of the publications in this group is 4. The 10 presented articles concern various aspects of rare diseases, reproductive genetics, and medical genetic counseling.

Contributions related to a successfully defended dissertation for the acquisition of the degree "Doctor" on the topic "Genetic counseling in patients with a probable tumor-predisposing syndrome"

The dissertation examines the possibilities for improving the diagnostic and consultative process in patients with hereditary oncological syndromes. In the context of modern precision oncology, early recognition of individuals with a genetic predisposition is essential for limiting morbidity and mortality through the implementation of individualized screening strategies. The study presents a comprehensive literature analysis of the epidemiology and mechanisms of development of the most common hereditary cancer syndromes, including Lynch, HBOC, Li-Fraumeni and others. A comprehensive study was carried out on the effectiveness of genetic counseling, the criteria for referral to molecular genetic tests, as well as the psychological impact of the results on patients and their families. The emphasis is on the importance of the multidisciplinary approach and the role of family history as a basic screening tool. Algorithms

for clinical behavior and follow-up have been developed in order to more effectively integrate genetic information into daily oncological practice.

Contributions in the field of "Oncogenetics and molecular diagnostics in oncohematology"

The presented book "The Genetic Code of Cancer" examines current trends in oncogenetics and its application in personalized medicine. The publication aims to connect complex scientific concepts with the practical needs of patients and their families. The mechanisms of carcinogenesis, the features of sporadic and hereditary forms of cancer, as well as the most common hereditary oncological syndromes, including Lynch syndrome and hereditary breast and ovarian cancer, are presented in detail. Significant attention is paid to medical-genetic counseling - from collecting a family history to the analysis and interpretation of next-generation sequencing (NGS) results. The psychological, ethical and social aspects of genetic testing are also considered, and practical guidelines for prevention and long-term follow-up are proposed. The book is a useful source both for people with increased hereditary risk and for medical specialists who strive for more effective communication and a deeper understanding of the genetic mechanisms of oncological diseases.

A series of studies [B4.7, D8.26] have shown that conventional cytogenetic analysis often fails to fully capture chromosomal instability in multiple myeloma (MM) due to the low mitotic index of plasma cells. The use of interphase fluorescence *in situ* hybridization (iFISH) has resulted in a significantly higher detection rate of prognostically significant genetic aberrations, such as del17p13 and IGH rearrangements, which are essential for identifying patients with a high-risk profile. The studies are based on statistical analysis of actual diagnostic tests performed in laboratory practice.

Cases of incidentally detected constitutional chromosomal abnormalities in the diagnosis of acquired hematological diseases have also been studied [B4.8]. As a result, an ethical and diagnostic approach has been developed for reporting such findings, which are important both for the patient himself and for the potential reproductive risks in his family. The implementation of FISH technology expands its application beyond oncohematological diseases, in order to identify various chromosomal disorders. The experience gained with the method creates a basis for the introduction of more informative approaches for biomarker analysis and stimulates the implementation of more comprehensive molecular panels, including MLPA, in routine diagnostic practice.

Contributions in the field of "Reproductive Genetics"

Based on eight years of practical experience covering over 17,000 cases, an analysis of the effectiveness of biochemical screening (BHS) in the first and second trimesters of pregnancy was performed. The higher sensitivity of the combined biochemical screening in the first trimester (CBHS1), which combines ultrasound markers and serum indicators such as PAPP-A and free β-hCG, in the detection of trisomy 21 was established.

A pioneering study for the country [B4.10, D8.20] was also conducted, examining the attitude of Bulgarian women towards non-invasive prenatal testing (NIPT). The results show that patients emphasize the safety of the method and the lack of risk of abortion, but often have inflated expectations regarding its diagnostic capabilities. This emphasizes the need for mandatory pre-analytical genetic counseling conducted by a medical genetics specialist.

It has also been proven that the implementation of NIPT leads to a statistically significant reduction in the number of amniocentesis performed solely due to advanced maternal age, while at the same time increasing the relative proportion of chromosomal abnormalities detected in other invasive diagnostic procedures [B4.3, D8.27].

Contributions in the field of "Dysmorphology and rare genetic diseases"

Original clinical observations and diagnostic approaches in rare syndromes characterized by significant clinical and genetic heterogeneity are presented. The importance of the *KMT2D gene* for the pathogenesis of Kabuki Syndrome [G8.30] is emphasized, as well as the role of international cooperation and the application of consensus diagnostic criteria for its more accurate clinical recognition. Both typical and atypical clinical variants of Cornelia de Lange Syndrome [G8.6] are described, emphasizing the systemic nature of the lesions and multiorgan involvement. Active participation in the development of national recommendations for monitoring and behavior in patients with neurofibromatosis type 1 and Noonan syndrome [G8.10, G8.31] is reflected, with the aim of standardizing clinical practice. Describing the 16p11.2 Duplication Syndrome [D8.25], the need for a comprehensive diagnostic approach based on intersectoral and interinstitutional cooperation, with the application of various genetic methods in resource-limited settings, including array CGH in children with unclear intellectual deficits and autistic spectrum behavior, is emphasized.

Contributions to genetic counseling, modern diagnostic methods, telegenetics and ethical aspects

An innovative study for Bulgaria has been conducted related to the transition to remote genetic counseling (telegenetics) [B4.14, D8.8]. The results show that online forms of counseling are preferred when discussing routine results, but cannot replace personal contact when reporting adverse findings or in complex cases of familial pathology.

The level of genetic literacy of patients regarding various tests, including thrombophilia tests, has also been analyzed [B4.12, B4.22]. It has been found that in the absence of qualified post-analytical genetic counseling, patients often overestimate the real risk, which leads to increased anxiety and unnecessary medical actions.

According to the academic reference prepared by the Library, MU-Varna, the scientific works of Dr. Mari Hachmerian have 7 citations.

Scientometric indicators and requirements

Indicator group	Minimum requirements of the ZRASRB for "Associate Professor"	Dr. Hachmerian - points	Dr. Hachmerian – implementation in %
A	50	50	100%
B	-	-	-
In	100	101,4	101,4%
G	200	219,9	110%
D	50	105	210%
Total	**400**	**476,3**	**119%**

According to the table above, Dr. Mari Hachmerian has a performance on the required indicators from 100 to 210%, an average of 119%, i.e. with her scientific production she covers the minimum number of required points.

Conclusion

The scientific activity of Dr. Mari Hachmerian-Andreeva covers a wide range of research - from fundamental developments in the field of oncogenetics to the creation of practical algorithms in prenatal and pediatric clinical genetics. These contributions support the development and consolidation of the personalized medical approach in the Bulgarian healthcare system, as well as the improvement of genetic prevention strategies at the national level. Her scientometric indicators fully cover the minimum required number of points for occupying the academic position of "Associate Professor" at the Medical University, Varna.

Considering all this, I take the liberty of recommending to the esteemed Scientific Jury to award Chief Asst. Dr. Mari Ara Hachmerian-Andreeva, PhD, the title of "Associate Professor" in professional field 7.1. "Medicine", for the needs of the Medical University - Varna.

Reviewer: /Prof. Dr. Ivanka Dimova, MD/

05/26/2026