### REVIEW

## of the PhD dissertation entitled:

"Genetic Counseling in Patients with Probable Tumor Predisposition Syndrome"

for obtaining the educational and scientific degree "Doctor"

Doctoral Program: "Medical Genetics"

Field of Higher Education: 7. Healthcare and Sports

Professional Field: 7.1 Medicine

Author: Dr. Mari Ara Hatchmerian-Andreeva

Supervisors: Assoc. Prof. Dr. Maria Levkova, PhD; Assoc. Prof. Dr. Eleonora Dimitrova, MD, PhD

Reviewer: Prof. Dr. Savina Petrova Hadjidekova, MD, PhD

Head of the Department of Medical Genetics, Faculty of Medicine, Medical University - Sofia

## General Overview of the Procedure and the PhD Candidate

The review was prepared in accordance with Order R-109-394/25.09.2025 of the Rector of the Medical University – Varna and Protocol 45/10.09.2025 of the Faculty Council. The submitted materials for the defense comply with the Procedure for obtaining the PhD degree at MU–Varna. The review follows the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB), its regulations, and the specific criteria for academic positions and scientific degrees at MU–Varna.

## **Brief Professional Biography of the Candidate**

Dr. Mari Ara Hatchmerian-Andreeva graduated with a Master's degree in Medicine from the Faculty of Medicine, Medical University 'Prof. Dr. Paraskev Stoyanov' – Varna, in 2011. In 2015, she obtained a Master's degree in Molecular Biology and Biotechnology. In 2017, she defended a PhD in Genetics on the topic 'Maternal Biochemical Screening as a Method for Prenatal Prevention'. The same year, she acquired a specialty in Medical Genetics at the same university.

Since 2018, she has been a Senior Assistant Professor at the Department of Medical Genetics, MU-Varna, and since 2019 has served as Head of the Laboratory of Medical Genetics at St. Marina University Hospital, Varna. Dr. Hatchmerian-Andreeva is a member of two international

scientific societies – the European Society of Human Genetics (ESHG) and the European Cytogeneticists Association (ECA) – as well as two Bulgarian organizations – the Bulgarian Society of Human Genetics and Genomics and the Bulgarian Pediatric Association.

She is the author and co-author of 48 full-text scientific publications and 71 published abstracts in international and Bulgarian journals. She has participated in four scientific research projects.

## Relevance and Significance of the Research

The dissertation addresses a highly relevant and socially significant problem – the assessment of genetic predisposition to malignant tumors and the role of medical genetic counseling in prevention and individualized patient care. In the context of the rapid development of molecular diagnostics and the implementation of personalized medicine, the topic is entirely up-to-date and contributes to strengthening the connection between clinical oncology and medical genetics.

# Structure and Content of the Dissertation

The dissertation is structured in accordance with the requirements for the PhD degree and demonstrates systematic organization, scientific consistency, and precision. It has a clear logical structure that guides the reader from the general context of oncogenetic syndromes to the specific research and analysis of the results. The terminology used is accurate and modern.

- Introduction clearly outlines the relevance and significance of the topic, motivates the choice of research subject, and defines the study's objectives.
- Literature Review comprehensive and well-structured, including up-to-date data from international and national sources. Subsections are logically arranged (epidemiology, classification, molecular mechanisms, diagnostic methods, and counseling). Contemporary references and international guidelines (ESMO, ASCO, NCCN, etc.) are appropriately cited, enhancing the scientific value of the work.
- Aims and Objectives concisely and clearly formulated; realistic and achievable.
- Materials and Methods thoroughly described, encompassing clinical, genealogical, laboratory, bioinformatic, and statistical approaches. The structure is transparent and reproducible.
- Results logically presented with appropriate graphics and tables. Subsections are well organized, facilitating the understanding of the different analytical stages.

- Discussion analytical and critical, comparing findings with international studies and highlighting the specific features of the examined population.
- Conclusion and Future Directions summarizes the main achievements and outlines opportunities for future research and clinical application.
- Findings and Contributions clearly formulated, specific, and justified by the results. Five main conclusions are derived, fully corresponding to the stated objectives. The identified contributions have both original and practical significance.
- Bibliography includes a substantial number of modern and authoritative sources presented in a consistent format.
- Appendices contain additional tables, figures, and materials that enrich the content and increase the practical value of the study.

### Publications Related to the Dissertation

In connection with the dissertation, the PhD candidate presents three full-text publications as first author, two of which are indexed in the Web of Science database. She also presents three conference papers and five abstracts related to the dissertation topic. These works fully correspond to the dissertation's thematic scope and include results from the conducted research.

### **Author's Abstract**

The author's abstract consists of 56 pages and accurately reflects the main sections and findings of the dissertation.

### Conclusion

In conclusion, the PhD dissertation of Dr. Mari Ara Hatchmerian-Andreeva, entitled 'Genetic Counseling in Patients with a Probable Tumor Predisposition Syndrome,' represents a high-quality, in-depth, and comprehensive scientific study distinguished by an exceptionally well-developed structure and methodological consistency.

The author successfully builds the dissertation on a solid theoretical and analytical foundation. Its structure reflects the logical progression of the research process—from scientific motivation and objective formulation through the selection of methods and data analysis to conclusions and contributions that have real practical significance for medical genetics and oncology.

Overall, the dissertation demonstrates maturity, independence, and professionalism. It combines a precise structure with profound scientific analysis, clarity of presentation, and tangible results of practical application. This combination reflects strong research competence and critical thinking.

The dissertation fully complies with the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB), its regulations, and the specific criteria for academic degrees at the Medical University – Varna.

Based on the above, I give a positive evaluation of the presented dissertation, the author's abstract, the achieved results, and the identified contributions. I propose to the honorable Scientific Jury to award the educational and scientific degree 'Doctor' to Dr. Mari Ara

Hatchmerian-Andreeva in the doctoral program 'Medical Genetics'.

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Prof. Dr. Savina Hadjidekova, MD, PhD