



OPINION

From: Prof. Anton Bozhidarov Tonchev, PhD - Head of the Department of Anatomy and Cell Biology, Medical University "Prof. Dr. Paraskev Stoyanov" — Varna.

On: dissertation for the acquisition of NSA "Doctor" on the topic "*PROGNOSTIC AND PREDICTIVE FACTORS IN GLIOBLASTOMA MULTIFORME*"

Dissertant: GEORGI STOYANOV STOYANOV, MD, Department of General and Clinical Pathology, Deontology and Forensic Medicine, Medical University — Varna, supervised by Prof. Dr. Petar Genev, PhD — Department of General and Clinical Pathology, Deontology and Forensic Medicine, Medical University-Varna

I am appointed to draw up an Opinion of Dr. Georgi Stoyanov's dissertation by order of the Rector of the Medical University — Varna R-109-71/04.02.2022 on the basis of an election by the Faculty Council of the Faculty of Medicine (Protocol No 59/28.01.2022), Medical University — Varna.

I. Biographical data for Dr. Stoyanov

Dr. Georgi Stoyanov Stoyanov was born in 1992 in Shumen. He graduated secondary school in his home city in 2011 and Medicine at the Medical University — Varna in 2017 with an award for high scientific achievements. In the course of his studies, Dr. Stoyanov is a four-year tutor in the Department of Anatomy and Cell Biology and in parallel two years in the Department of General and Clinical Pathology, Forensic Medicine and Deontology of Bulgarian and English-speaking students, with a profile of medicine, dentistry and pharmacy. During his studies, he was a member of ASMB-Varna, respectively Secretary (2014-2015) and Deputy Chairman (2015-2016) of the organisation and member of the Board of Control and Quality at national level (2015-2016), as well as a member of the BSYSB Organising

Committee (2014-17), where he organised the scientific programme and was responsible for the editorial team.

After his graduation, Dr. Stoyanov started working as a part-time assistant at the Department of Anatomy and Cell Biology and the Department of Physiology and Pathophysiology, the Management Board of Pathophysiology, where he conducts exercises in Bulgarian and English for students of medicine and dentistry. In 2018 he was appointed as a co-ordinator and later a resident in General and Clinical Pathology at the clinic of University Hospital St. Marina — Varna and regular assistant prof. at the Department of General and Clinical Pathology, Forensic Medicine and Deontology at Faculty of Medicine, Medical University — Varna. In 2019 he started working on the current PhD, in regular form, successfully receiving and authorised by the Committee on Ethics of Research, Medical University-Varna, in connection with the activities set out in the dissertation work.

The scientific interests of Dr. Stoyanov are diverse, focused mainly on pathology of the central nervous system, anatomical structures and diseases in the field of the head and neck, autopsy and infectious pathology. As evidence of the quality of his scientific work there are more than 80 full-text scientific work, in its majority in English published in international indexed journals. The candidate's work has been cited more than 350 times, given the short period of publication, and his personal impact factor is over 25. Dr. Stoyanov has also published a chapter in the international textbook - Handbook of Clinical Neurology. The candidate has successfully completed four courses to Web of Science and is a member of the editorial board of the Cureus Journal of Medical Science, an international indexed journal.

Beyond the scientific work, the applicant's expertise is well highlighted through reports of rare cases, mostly autopsy, and Dr. Stoyanov also holds two specialised work certificates -The clinicalAutopsy with a module for biobanks, issued by the University of Oviedo, Spain and MMR/MSI professional expert course of Targos Molecular Pathology GmbH.

II. General data on Dr. Stoyanov's thesis

Dr. Stoyanov's dissertation work extends over 95 standard printed pages (not including bibliography). The text is distributed in an introduction, 7 thematic chapters, contributions and publications related to work. The data obtained and the analyses carried out are illustrated by 65 figures and 13 tables. The literature review contains 250 titles from Bulgarian and foreign authors.

III. Assessment of the relevance of the topic

Glioblastoma multiforme (GBM) is a malignant neoplasm of the central nervous system. GBM is one of the most malignant tumors in human pathology, with minimal progress in patient survival in the last 50 years despite huge efforts to uncover molecular mechanisms on the basis of which to create a therapeutic approach. Most often, GBM is not subject to radical surgery and chemotherapy and radiotherapy are not effective enough to suppress the tumour for a period longer than several months. Therefore, the discovery of new molecules in the pathogenesis of the GBM would lead to their use as new biomarkers or a basis for a therapeutic approach. This makes Dr. Stoyanov's analysis in the current dissertation work extremely relevant from a fundamental and clinical point of view.

IV. Evaluation of the Introduction and Literature Review

The introduction clearly motivates the need for research in the field of dissertation work. The literary review shows the dissertant's good awareness of the abundance of literary sources on the topic of anatomical variations. Historical aspects of the development of pathology science in the field of GBM have been examined and Bulgarian contributions in the area have not been missed. A detailed classification of glial tumors with a focus on GBM is presented. The Literature review would benefit in addition by complementing the characteristics (classifications) defined in recent years by sequencing the transcriptome of single glioblastoma cells.

V. Assessment of the Aim and Objectives

The Aim and the Objectives are clearly formulated. Given the methodologies presented, I value the Aim as an achievable one.

VI. Evaluation of the Materials and Methods section

The materials and methods are described in detail in such a way as to allow the experiments to be repeated by independent researchers. Histological material is used from the clinic where

Dr. Stoyanov works after obtaining ethical consent in the appropriate manner. I give a high value to the methods used, including innovativeness, and their description.

VII. Evaluation of the Results section

The results are illustrated by 46 figures and 13 tables of good quality that clearly visualise those of the thesis. Particularly impressive is the application of a new global molecular marker in GBM - Diaph3. I accept that the results thus presented support the conclusion of the Thesis.

VIII. Assessment of sections Discussion/Summary/Conclusions

The Discussion presents with published results in the light of in-depth synthesis of known data in literature, including in relation to the molecular classification of GBM, IDH mutational status, demographic and clinical characteristics of the cohort of patients, MGMT mutation status, and the role of the newly proposed marker of GBM - Diaph3. In a self-critical approach, restrictive aspects of dissertation work have been addressed.

The conclusions are formulated in 5 aspects, reflecting the more important results achieved by the dissertant. I consider the Conclusions thus presented to be consistent with the results.

IX. Assessment of the contributions of the thesis

I accept the summaries of the dissertation work of diagnostic and clinical-therapeutic nature. I believe that the work on the thesis is the personal achievement of the Ph.D. student, and the contributions are sufficient to acquire the degree "Doctor in Medicine".

X. Evaluation of publications related to the thesis

Presented are 2 publications in referenced (in world databases) journals with impact factor and 6 publications in referenced journals without an impact factor. Dr. Stoyanov is the first author to all these papers, which once again confirms that the thesis is his personal achievement.

Conclusion

The PhD thesis of Dr. Georgi Stoyanov Stoyanov, MD from Department of General and Clinical Pathology, Deontology and Forensic Medicine, MU-Varna is dedicated to an extremely important problem for fundamental science and the clinic. I believe that the dissertation work fully complies with the Act on the Development of the Academic Staff of the Republic of Bulgaria and academic staff Regulations of the Medical University-Varna for the acquisition of the degree “Doctor in Medicine”. That is why I will vote positively and allow myself to recommend the same to the other members of the honorable Scientific Jury, designated by Order R-109-71/04.02.2022 of the Rector of the Medical University-Varna.



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Varna, 17.03.2022