

## REVIEW

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**SUBJECT:** COMPETITION for the academic position of "Associate Professor" in General and Clinical Pathology, in the field of higher education 7. Health and sports, professional field 7.1. Medicine, published in the State Gazette / no. 53 of 12.06.2020/ and on an approved proposal by the Faculty Council of the Faculty of Medicine / ex. No. 26/13.07.2020/ for the needs of the Department of General and Clinical Pathology, Forensic Medicine and Deontology at MU-Varna.

With a decision from a meeting of the Faculty of Medicine at MU-Varna under protocol No. 26/13.07.2020 and with order No. P-109-305 /07.08.2020 of the Rector of MU-Varna, I was elected a member of the Scientific Jury, and based on Protocol No. 1/17.08.2020 of the meeting of the SJ, I was appointed to prepare an official resume on the procedure for obtaining the academic position of "Associate Professor", with a candidate Dr. Deyan Lyudmilov Dzhenkov, MD.

The only candidate participating in the competition for the academic position of "Associate Professor" in the Department of General and Clinical Pathology, Forensic Medicine and Deontology at MU-Varna is Dr. Deyan Dzhenkov, MD. According to the regulations of the competition, the candidate has submitted a complete set of materials on paper and electronic media, including all necessary documents following the requirements of ZRASRB, the Regulations for its implementation, and the Regulations for the development of the academic staff at MU-Varna. All other required documents are up-to-date and follow the requirements.

#### **Brief biographical data and career development of Dr. Deyan Dzhenkov, MD.**

Dr. Deyan Lyudmilov Dzhenkov was born on March 31, 1973 in the city of Dobrich. He graduated from high school in 1991 at the High School of Natural Sciences and Mathematics "St. Kliment Ohridski" in Silistra with main subject biology. In 1992 he was admitted to the Thracian University, Faculty of Medicine - Stara Zagora, where in 1999 he acquired a Master's academic degree in medicine / diploma No. 2239/04.11.1999/. In the period 10.12.1999 - 20.03.2006. Dr. Dzhenkov worked as a doctor-ordinator in the Pathological anatomy department of General hospital Silistra AD. On March 21, 2006, he was hired and to this day works at the General and Clinical Pathology Clinic of the University Hospital "St. Marina" – Varna as a pathoanatomist, and in the relevant department of MU-Varna as an assistant. In 2010-2014 he was a faculty advisor, and since 2014 - an administrative assistant at the Department of General and Clinical Pathology, Forensic Medicine and Deontology. Dr. Dzhenkov acquired a specialty in General and Clinical Pathology in January 2008/ No. 013491/18.02.2008/. In 2019 he acquired a PhD diploma in the scientific specialty Pathologoanatomy and Cytopathology after defending a dissertation on "Expression of the Transcription Factor ZBTB20 in Glial Tumors of the Central Nervous System" / diploma No. 340/23.05.2019/, MU-Varna.



Dr. Dzhenkov has certificates for the completion of a number of courses, like: PD-L1 Testing, Expert Course in NSCLC, Expert course in Urothelial carcinoma; Expert course in Head and Neck carcinoma; / in Cassel, Germany, in 2017, 2018, and 2019/; Course in HER2 DISH-test diagnostics in mammary gland and stomach carcinoma, 2018 in Varna; Additional qualification with a certificate of pedagogical qualification of educators from health institutions / Certificate CДО-99-296/12.07.2012 /; European school in pathology of the urinary tract and the male reproductive tract, 2018, Varna; "Educational Basis of Academic Teaching of Project BG051P003-3.1.09-0013 "Creating a Modern System for Career Development of Educators at MU "Prof. Dr. Paraskev Stoyanov" - Varna."

Dr. Dzhenkov participated as an author in 46 scientific articles with a total of 300 pages, published in national and international journals. His professional and scientific interests are mainly in the field of neuropathology and molecular biology.

Dr. Dzhenkov has an experience of 20 years and 7 months as a doctor /By 31.07.2020, ref. No. Y-1095/, and 14 years and 4 months as an educator / Certificate No. 099-2296/24.07.2020/. The candidate is fluent in English and has the necessary computer skills. He is a member of the BMA and the Bulgarian Pathology Association.

## **II. Description of indicators to measure Dr. Deyan Dzhenkov MD's scientific performance.**

In order to participate in the competition for "Associate Professor", Dr. Deyan Dzhenkov has presented a total of 36 full-text scientific publications, not related to the dissertation, including:

- **11 publications equaling a monograph**, referenced and indexed in world-famous databases /Scopus and Web of Science/; **9 publications** referenced and indexed in the same databases, **13 publications in unreferenced journals with scientific peer-review** and collections, and **3 publications** outside the minimum requirements.

Note: In the above stated number of publications in unreferenced journals was omitted the number of the first full-text article, containing evidence material and included in all lists below, incl. those, referring to contributions. The article's authors are Tzaneva M, Dzhenkov D. Ivanov K., its heading is „ Morphological and histochemical study in gastric carcinoma in young persons, Tr.J. of Sci, 2009, /supp. 1/, 46-49, ISSN 1312-1723, and it takes part in the calculations for the formation of the number of points of this group of publications.

Dr. Dzhenkov's PhD dissertation on "Expression of the Transcription Factor ZBTB20 in Glial Tumors of the Central Nervous System", defended in 2019, was presented and evaluated by the SJ, which gives a reason to believe that, according to ZRASRB, criterion A of the minimum requirements for obtaining the academic position of "Associate Professor", is met.

The main direction of Dr. Dzhenkov's scientific work, and to which he has dedicated his dissertation, focuses on researches aiming to define the relative share, frequency, demographic characteristics, and morphological diagnostics of glial tumors, and more specifically, of the most common malignant CNS tumor - the glioblastoma multiforme. Along with defining these characteristics, there is the clarification of the molecular mechanisms regulating the process of development of the tumor, which, in turn, would be extremely helpful in finding a way to slow down the progression of this aggressive tumor. In this regard, Dr. Dzhenkov has completed the assigned task to study and define the expression of the transcription factor ZBTB20 in different glial tumors of



the CNS, in order to find a relation between the expression of this marker and the survival of patients with glial tumors, as well as its correlation with certain prognostic and predictive factors of the disease.

**Eleven of the publications, presented by Dr. Dzhenukov**, referenced and indexed in world-famous databases, **equal a monograph**. Most of them are related to tumors of the CNS, mainly to glial tumors, and more specifically, to the glioblastoma multiforme, characterized by extreme aggressiveness. /№№ 1a, 2a, 3a, 5a, 6a, 10a and 11a/. The fact that some of the publications are a sequel of the developments used in the PhD dissertation, leaves a good impression.

With Dr. Dzhenukov's active participation, the cellular biology of the glioblastoma multiforme has been thoroughly studied /publication 1a/, presenting with a wide range of genetic and epigenetic changes, allowing for an increased number of mutations, some of which play a specific part in patients' survival and response to the performed treatment. It has been noted that the changes in the genetic information, compared to its physiological levels in "healthy" astrocytes, are the reason for the cellular and extracellular reorganization, followed by different manifestations in their biological and morphological forms. This fact allows Dr. Dzhenukov to join the imposed opinion of a number of authors, considering that the term "multiforme" is justified in the 21 century, having acquired a new popularity on the grounds of the genotype diversity of the tumor.

The correlation between the expression of Ki67 in the cells of glial tumors with different levels of differentiation /according to WHO's classification/ and patient survival have been tracked /publication No.2a/. The development's results show that the average percentage of Ki67 positive nuclei in the tumor cells of the glioblastoma multiforme is not associated with and cannot be used as an evaluation of survival, and at the same time it is an important immunohistochemical index for defining the level of differentiation of the glial tumors.

Dr. Dzhenukov et al. have directed their attention to the whole "diverse" group of intracranial tumors, including benign and malignant, primary and metastatic tumors, presenting with a diverse histological prospect and IHC-profile of the different types, whose understanding is of extreme importance for the correct diagnosis. This allows the authors to suggest the development of a diagnostic algorithm, based on the tumor location, the histological finding, and its immunohistochemical profile, which may be extremely valuable in diagnosing small materials from the deep brain layers or tumor fragments. /No. 3a/.

The diagnostic value of epithelial markers AE1/AE3, and EMA is evaluated, which sometimes give a positive expression in cells of glioblastoma tumor tissue. Dr. Dzhenukov pays attention to some authors' assumption that, although unlikely, there are cases when glioblastomas can produce keratin molecules, which in turn requires the use of a wide range of antibodies, regarding the differentiation of the glioblastoma multiforme from carcinoma metastases. /5a/.

The presented concept of the historical development of GBM is reviewed. It follows the descriptions of the tumor made through time, starting with the first one, made more than 200 years ago by Berns /in 1800/, marks the significance of the best description of a GBM histological finding made in 1865 by Virchrov, and ends with the publications reflecting the present state of the knowledge of the glial tumors' biology and molecular characteristics /6a/.



A rare case is described of complications with a low-malignancy glioma with a developed destruction of the dura and the calvaria, with a lack of preceding surgical intervention or radiotherapy /10A/ at the same time making a thorough analysis of literature.

An extremely rare case is presented /No 11a/ of papilloma of choroid plexus in the 4-th brain ventricle, in multiple pregnancy of a 27-year-old woman, with a miscarriage in the second trimester. An exact macroscopic description is made and the changes and findings which caused the miscarriage are photographed.

In a publication included in the group of monograph-equal publications, according to data of the Pathology clinic at University hospital "St. Marina" - Varna, a thorough and systematic analysis has been made over a 4-year period of tumors, developed in the head and neck area /4a/. Defined are the demographic characteristics, the relative share of different localizations, and the histological findings of the above-mentioned tumors. It must be noted that the received results are identical to those published by the National Oncology Institute, which is a sign of the representativeness of the data of a single institution.

Two of the 11 publications refer to diseases in the GIT. An autopsy case is described of a patient clinically and radiologically diagnosed perimortem with chronic obstructive lung disease /No. 8a/, who, without a biopsy, has been diagnosed with a lung carcinoma. The autopsy established attenuated familial adenomatous polyposis and colorectal carcinoma with multiple metastases in the lungs, liver and brain. The authors state the need for a complete and complex testing of patients in case of a refusal or impossibility of a biopsy. The second case presented is that of a 60-year-old male patient with an atypically developing syndrome of Trousseau with a pancreatic carcinoma, presenting with a migrating, recurrent thrombophlebitis dating back 6 months; multiple thromboses of abdominal veins, veins of lower limbs, and massive pulmonary thromboembolism which lead to a fatal episode /7a/.

A rare case of ameloblastoma of a 43-year-old woman is described /No.9a/, where, 10 years after the tumor resection and the adjuvant radiotherapy, metastases developed in the lungs. The immunohistochemical tumor profile, the clinical picture, and the therapeutic behavior confirmed the diagnosis of ameloblastoma.

In total, the number of points from the presented publications is 163,45, with a required minimum of 100 points. This defines criterion B of the minimum requirements for taking the academic position of "Associate Professor" according to ZRASRB as met.

From the 9 publications listed by Dr. Dzhakov, referenced, and indexed in world databases /SCOPUS and WEB of Sciences/, I accept 8 full-text publications - articles No. 1, 2, 3, 5, 6, 7, 8, 9 from the minimum requirements list for criterion D. Article No. 4 is identical to No.8 in the list of 11 monograph-equal publications. Of the non-referenced journals for covering the minimum requirements for criterion D, I accept all 12 articles in the list, in addition to the full-text article 13, which has been omitted for technical reasons probably /listed in a note/, as well as the three articles from the full-text publications list, out of the minimum requirements for associate professor.

The number of points from publications referenced in world databases are 111,02, which, together with the points from non-referenced in world databases publications, 92,07, sum up to





203,09 points. This number is enough to cover criterion D of the minimum requirements for the academic position of "Associate Professor" according to ZRASRB /the minimum number of points required is 200/.

The scientific communications presented by Dr. Dzhenkov at national and international forums, congresses, and conferences are 15, and there is no data as to which of the forums are national and which are international.

Dr. Dzhenkov has 42 citations, of which 34 are in scientific journals, referenced and indexed in world databases; 2 citations are in monographs and collective volumes with review, and 6 are in non-referred journals /academic reference from MU-Varna No. 512/03.08.2020 for citations by Bulgarian and foreign authors/. This gives grounds to assume that criterion D is fulfilled.

The presented scientific publications show that Dr. Dzhenkov is the first author in 2 of them /7.9%/; he is a second author in 7 publications /24.1%/; third author in 11 /30.6%/ and consecutive author in 9 publications. This shows a significant personal contribution by the author to the scientific research presented in his scientific communications. It is impressive that Dr. Dzhenkov's research was carried out in collaboration with a wide range of specialists - a fact that testifies to interdisciplinarity of the author's scientific interests. The reference made by Dr. Dzhenkov about the main fields of his scientific work shows that they are oriented mainly in the following areas:

1. Publications related to CNS tumors, with accent on glial tumors
2. Publications related to tumors outside the CNS
3. Publications describing morphological changes of some non-tumor diseases
4. Publications of cases and research methods from the clinical and autopsy /incl. forensic/ practice and research related to the technical possibilities of different video-registry means and their application contributing in a diagnostic, clinical, and educational aspect.

#### **Evaluation of the contributions of the scientific works of Dr. Dzhenkov, MD.**

##### **A. Contributions of publications in the field of CNS tumors /glial tumors/**

The reference of the contribution of Dr. Dzhenkov's scientific work shows the various interests of the author and his ability to work together in a team of specialists for different fields of science. I consider most significant the contribution of publications related to CNS tumors, with accent on glial tumors. Therefore, the first comprehensive clinically-morphological, immunohistochemical, and statistical analysis of primary and metastatic tumors in patients operated at the neurosurgical departments of both general hospitals in Varna, which serve the whole north-eastern Bulgaria, is of great scientific and practical importance. The first in Bulgaria analyzed expression of ZBTB20 in the nuclei of glioma tumor cells has a scientific contribution and original character in relation to the general survival rate of patients, as well as the evaluation of ZBTB20 and Ki67 as prognostic factors of the general survival with the mentioned tumors, with a different level of differentiation. Based on the diffuse expression of tumor cells of the ZBTB20 gene, there is an assumption that the marker may have a diagnostic value and therapeutic significance as an aim of the antitumor treatment.

A contribution of scientific and practical character is the first in Bulgaria parallel research on the frequency and epidemiology of intracranial primary and metastatic tumors of the CNS in Bulgaria and Brazil. The results show that primary tumors mostly affect patients from Brazil - 86.45%, whether in



Bulgaria their number is smaller - 69.17%; and vice versa - metastatic tumors among Brazilian patients are 13.55%, whether in Bulgaria their number is significantly larger - 31.28%.

Confirmative is the establishment of positive expression of epithelial markers like CK AE1/AE3 and EMA in glioblastoma tumor cells, which requires the inclusion of other antibodies in a broad immunohistochemical panel in order to differentiate glial tumors from carcinoma metastases.

#### **B. Contributions from publications, related to tumors outside the CNS.**

A confirmative contribution in this area is the statistical research carried out in Bulgaria for the first time of head and neck tumors, distributed by localization and histological type /publication No 4a, presented in the group of monograph-equal publications/. Confirmative are the contributions from publications No 1c, 2c, 4c, and 5c, referring to: 1c. Tracking the morphological and histological changes with gastric carcinoma in young individuals with prevailing development of diffuse carcinoma and precursor lesions adjacent to the tumor, described in familial gastric carcinoma; 2c. Described is expression of chromogranin A in diffuse gastric carcinoma, with the supposition that in the process of carcinogenesis some of the tumor cells may acquire endocrine phenotype; 4c - contribution to a rare type of pancreas NET, localized in the processus uncinatus, and 5c - a publication related to a research on histologically confirmed esophageal malignancies in a health institution /St. Marina University hospital - Varna/, with statistical distribution by localization, histological type, and demographic data of the patients; a confirmative contribution is the established tendency for leveling carcinoma frequency to that of developed countries.

#### **C. Contributions in publications related to the morphology of non-tumor diseases**

First of all, these are publications of a scientific-practical contribution, related to the gynecological practice. Here is referred a case of fulminant generalized peritonitis, caused by *Prevotella bivia* /7b/, and the review on avascular pelvic spaces and their meaning and application in gynecological practice /10c/.

Secondly, these are publications related to pediatric practice. Two autopsy cases of cystic fibrosis with polyorganic impact, including kidneys, are presented /3b/; a case creating differential diagnosis obstacles in the pediatric patient with blue scleras and impaired development of the trabecular bones with contractures, without fractures or genetic examinations /12 c/, and a case of Potter sequence in diamniotic twins /4 b/.

A publication of scientific and practical contribution is that which has studied the histological basis for the development of Frank's sign, related to cardiovascular disease /9b/ and with a potential representing an early sign for the development of cardiac damage.

A small part of Dr. Dzhankov's publications are dedicated to rare clinical cases with different localization, like the cases related to the advanced syndrome of the empty nose in a patient with a number of surgical interventions as a result of osteomyelitis in the upper jaw /2b/ and a case of acute necrotising encephalitis of the upper airways /13c/.

**D. Scientifically applicable contributions in publications related to cases and research methods from clinical and autopsy practice with an accent on the diagnostic, clinical, and educational aspect.**



Presented are cases and research methods from clinical and autopsy practice with a contribution in a diagnostic, clinical, and educational aspect in the full-text publications No. No. 5b, 3c, 7c; 8c; 9c; 11c. Rare diseases and their morphological finding are discussed, like an autopsy case of pontocerebellar hypoplasia /3c/; a clinical case of the first reported in Bulgaria chylous ascites after laparoscopic myomectomy /5b/ and a case of early changes with retrorenal fibroplasia in a newborn /9c/.

Contributing to practice are the studied possibilities for performing a high-rotation cellular block of effusions and its application in the diagnostics of malignant effusions, incl. an immunocytochemical testing of a patient with tissue biopsy contraindications /7c/.

Two publications discuss the issue of video documentation in autopsy practice, following the most suitable types of technical means for video documentation, which offer the best quality of picture, sound, and price /8c, 11c/. Questions are raised of the application of such documentation as judicial evidence and educational materials in seminars for students and graduates.

#### **Evaluation of the participation of Dr. Dzhenkov in research and teaching**

From the reference for Dr. Dzhenkov's study load, it can be seen that for the presented 5 years /2015/16 - 2019/20/, according to the normal limits of the workload at MU-Varna for non-habilitated lecturers, which was 220 hours, Dr. Dzhenkov worked more hours, except for 2015-2016, when his workload was 210 hours. Dr. Dzhenkov also has practical classes in medicine, dental medicine, and pharmacy in Bulgarian and English, and participates in the preparation of tests and electronic study resources. Dr. Dzhenkov is the leader of intra-university project No 19010/\_2019 in MU-Varna on the topic: "Predictive and Prognostic Markers in Glioblastoma Multiforme". By order of the Rector of MU-Varna of March 17, 2017, Dr. Dzhenkov is appointed leader of the specialization in General Clinical Pathology of Dr. Georgi Stoyanov Stoyanov, based at the Pathology clinic at the University hospital „St. Marina“ - Varna.

#### **Conclusion:**

The candidate for the academic position "Associate Professor", Dr. Deyan Lyudmilov Dzhenkov, is a confirmed, respected, and excellently prepared specialist with many years of professional and educational experience, an accurate diagnostician, and a profound scientist - qualities which help him work in a team and combine his versatile scientific interests with clinical practice. The scientific production presented by the candidate is a clear evidence of his versatile interests in different areas of medicine. I believe that Dr. Dzhenkov fulfills all the necessary requirements and criteria, as well as the quantitative science measurement indicators of the Regulations for the development of the academic staff at MU-Varna in order to take the academic position "Associate Professor". Having in mind the above reasons, I confidently give my evaluation "YES" and suggest that the respected members of the SJ vote positively for awarding Dr. Deyan Lyudmilov Dzhenkov, MD, the academic position "Associate Professor" in General and Clinical Pathology for the needs of the Department of General and Clinical Pathology, Forensic Medicine and Deontology at MU-Varna.

07.10.2020

Reviewer:

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