



REVIEW

regarding the competition for associate professor of gastroenterology in the Department of "Internal Diseases" of the Faculty of Medicine of the University "Prof. Dr. Asen Zlatarov", Burgas, announced in the "State Gazette", issue 45, dated June 17, 2022.

by Prof. Dr. Iskren Kotsev, MD, Medical University, Varna, MBAL-Varna

By Order No. RD-269/15.09.2022 of the Rector of the University "Prof. Dr. Asen Zlatarov", Burgas, I was appointed to participate in the Scientific Jury for the above-mentioned competition, and following the first meeting of the Scientific Jury, I was appointed to present a review.

For the competition for an associate professor of gastroenterology announced in the "State Gazette" issue 45 of June 17, 2022, only Dr. Milko Bozhidarov Mirchev, MD, head of the Department of Gastroenterology at the Medical Center "Heart and brain", Burgas submitted regular documents within the deadline. The assessment and the final opinion are based on the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria of May 21, 2010, the Regulations for its Application of September 24, 2010, incl. all additions until July 19, 2022 and the Regulations for the development of the academic staff at the University "Prof. Dr. Asen Zlatarov", Burgas.

Associate Professor Milko Bozhidarov Mirchev has the scientific and educational degree "doctor" after successfully defending a dissertation in the scientific specialty of gastroenterology in 2011 on the topic "Clinical significance of microsatellite instability and promoter methylation of DNA in colorectal carcinoma", with a published monograph "Hereditary neoplastic syndromes in gastroenterology" and with habilitation as an associate professor in 2015 at the Medical University, Varna. Assoc. Prof. Mirchev completed secondary education in 1996 at the I Language High School, Varna and graduated as a Master of Medicine in 2002 at the Medical University "Prof. Dr. Paraskev Stoyanov", Varna. After winning a competition in the period 2003/2007, he was a full-time doctoral student at the "Internal Diseases" Department, Gastroenterology Clinic, Medical University, Varna. Since 2007, he has been working as a resident physician at the Gastroenterology Clinic, UMBAL "St. Marina", city of Varna. Since 2009, he has been a gastroenterology specialist at the Gastroenterology Clinic of UMBAL "St. Marina", city of Varna. In 2011, after a successful defense of his dissertation, he was awarded the educational and scientific degree "doctor" in scientific specialty: 03.01.14 "gastroenterology". In 2014, he acquired a specialty in gastroenterology. From September 2016 to April 2022 Assoc. prof. Mirchev is the head of the Gastroenterology Clinic at the "St. Marina", Varna, and from 11.04.2022 he was appointed as the head of the newly formed

Department of Gastroenterology at the "Heart and Brain" Medical Center, Burgas.

Assoc. prof. Mirchev has 20 years of medical experience, 11 years of teaching experience - one academic year as a part-time assistant, and since 2013 as a chief assistant in the Gastroenterology Clinic. He has been an associate professor for 7 years, and for 6 years he has been working as the head of a clinic.

Research activity

In 2011, Associate Professor Mirchev successfully defended his thesis in the scientific specialty of gastroenterology on the topic "Clinical significance of microsatellite instability and promoter methylation of DNA in colorectal carcinoma", referred for defense by the Department of Internal Medicine of the Medical University, Varna. The main contributions of Assoc. Prof. Mirchev include the development of an approach for patients with sporadic, familial and hereditary colorectal carcinoma. In his thesis, he performed the largest Bulgarian study on microsatellite instability and DNA methylation in colorectal carcinoma, introduced a quantitative pyrosequencing method to determine methylation in the promoters of some genes. It confirmed the notion of different carcinogenesis of proximal and distal colorectal carcinoma and demonstrated the importance of microsatellite instability and DNA methylation as prognostic factors in these patients. Assoc. Prof. Mirchev created a consultation office for patients with hereditary diseases and a register of examined patients. Assoc. Prof. Mirchev defended for the second time in Bulgaria, after Dr. Kalaidjieva, a dissertation on genetic changes in colorectal carcinoma, and for the first time on the role of methylation in the carcinogenesis of colorectal carcinoma.

During the realization of his scientific thesis, Prof. Mirchev established himself as a rapidly advancing specialist in the field of oncology and gastroenterology. He specialized for 6 months in Bonn, Germany, in connection with his dissertation. Dr. Mirchev has also completed specializations in Switzerland and Great Britain.

In addition, assoc. Prof. Mirchev is the author of the monograph "Hereditary neoplastic syndromes in gastroenterology" from 2015, in which he examines the current state of clinical genetics in the field of neoplastic gastroenterological syndromes and shares his experience in this field. The monograph is of great interest to modern gastroenterological science and practice. In it, the author examines current aspects in genetics, clinical presentation, diagnosis, approach to patients and the possibilities for early detection and prevention of hereditary carcinomas of the stomach, small and large intestine and pancreas. The role of genetic counseling to cover relatives and their adequate follow-up with the aim of prevention and early diagnosis is described in detail. Also, original works from his pioneering dissertation, Clinical Significance of Microsatellite Instability and Promoter DNA Methylation in Colorectal Carcinoma, are included. Assoc. Prof. Mirchev is an experienced clinical physician, routine endoscopist, developing

significant activity at the Gastroenterology Clinic at that time. He brings extensive clinical, endoscopic and scientific experience. The author is one of the few medical professionals who have worked extensively and simultaneously in modern gastroenterology, gastrointestinal endoscopy, and clinical genetics, making personal and original contributions to each of these fields. His monograph fills a gap, making a significant contribution to the modern medical literature and is of interest to a wide range of medical specialties - general practitioners, engineers, gastroenterologists, surgeons, paediatricians, geneticists, interns and medical students. It is still today the best manual in the field of clinical gastroenterological genetics, including the current state-of-the-art and the author's personal experience. It is an indispensable guide for all those interested in and working in this field of clinical gastroenterology.

Prof. Mirchev has an impressive scientific and research activity. 46 of his scientific works have been published in extenso - 1 dissertation, 1 monograph and 44 scientific articles, of which 15 are in Bulgarian and 29 in English. 20 scientific works have been published in scientific publications, referenced and indexed in world-famous scientific databases (Scopus; Web of Science). They include the following renowned journals: Gut, Hepatogastroenterology, Journal of Probiotics and Health, Frontlines in Clinical Drug Research, Target Oncology, Journal of International Medical Research, Gastrointestinal Disorders, Genes, Journal of Clinical Oncology, Annals of Oncology, Journal of Crohn's and Colitis, Current Oncology, International Journal of Molecular Medicine, European Review for Medical and Pharmacological Sciences, Folia Medica, Journal of the Balkan Union of Oncology.

From a total of 46 scientific papers, dr. Mirchev is the first author in 15 of them, the second author in 9, and the third and next in 22. 20 of all publications are in international journals with an impact factor. Assoc. Prof. Mirchev's scientific works have been cited 43 times. 6 of his scientific works in English have been cited 34 times in renowned international scientific journals and foreign databases. With the highest number of citations is the scientific article «Risk and protective factors for the development of colorectal polyps and carcinoma (Bulgarian experience)», followed by «DNA methylation in patients with colorectal carcinoma - correlation with some clinical and morphological characteristics and local tumor invasion». The total impact factor of his scientific publications is 30.645. From a total of 25 publications in textbooks, anthologies and refereed journals, Prof. Mirchev is the first author in 13 of them (52%).

His scientific works are in the following areas: clinical, genetic and epigenetic studies in colorectal carcinoma; promoter methylation; polyposis of the gastrointestinal tract; gastrointestinal oncology; endoscopy; Helicobacter pylori; IBD etc.

His main contributions are in the field of clinical genetics, carcinogenesis of colorectal carcinoma, endoscopy and gastrointestinal oncology.

Prof. Mirchev in his publications shows himself as an original, up-to-date and conscientious researcher.

He participated in 4 scientific projects:

1. FFNNIPO_12_01078 - "Prevention of colon neoplasms through early diagnosis of precancerous lesions and carcinomas in the stage of intraepithelial neoplasia". Scientific Research Fund, Ministry of Education, Youth and Science, 2012-2013;
2. "Modern diagnostic and therapeutic approach in patients with hepatocellular carcinoma. "Medical Science" Fund, Medical University - Varna;
3. Pilot Study for the use of microRNAs and circulating tumor DNA as prognostic and follow-up biomarkers in gastrointestinal cancer patients - 2015;
4. Evaluation of expression levels of selected microRNAs as potential biomarkers in children and adolescents with inflammatory bowel diseases.

The main scientific contributions of Assoc. Prof. Mirchev are:

- Conducted the largest study in Bulgaria on the role of microsatellite instability and DNA methylation in patients with CRC
- A complex approach was developed for patients with sporadic, familial and hereditary colorectal carcinoma (CRC)
- Introduces a quantitative method (pyrosequencing) to determine methylation in the promoters of some genes
- Confirms the existence of a group of tumors with simultaneous methylation of several genes (CIMP-phenotype) and defines a clinico-morphological characteristic specific to it
- Confirms the notion that proximal and distal colorectal carcinomas have different pathogenesis
- Proves the importance of MCH and DNA-methylation as prognostic factors in CRC patients
- Creates an office and registry for counseling patients with hereditary bowel diseases.
- Introduces in the Clinic of Gastroenterology criteria for quality conduct of endoscopic examinations of the gastrointestinal tract using NBI and magnifying endoscopy for early detection of carcinomas in the esophagus and stomach, Barrett's esophagus, intubation of the terminal ileum, use of a hat to view the intestinal folds
- Participated in a study of the probiotic *Lactobacillus reuteri* in the eradication of *Helicobacter pylori*
- Participated as a co-investigator and coordinator in a number of multicenter national and international phase 2b, 3 and 4 clinical trials in the diagnosis and treatment of patients with chronic hepatitis C, NSAID-induced gastropathy and inflammatory bowel diseases
- Participated as reviewer of articles in *Journal of Clinical Epigenetics and Scripta Scientifica Medica*

Scientific activity

Prof. Mirchev has an enviable scientific activity - he participated in 23 national and international scientific forums with scientific announcements, reports or posters, which speaks of the high level and activity of his scientific activity. He has given 17 oral reports, including 4 reports in English, at international scientific forums in Berlin, Paris, Sofia and Varna.

He has repeatedly participated in scientific forums of UEGW, EAGEN, ECCO, BDGE, Gastroforum Varna Novosti.

The spectrum of his scientific activity is quite broad and includes – clinical genetics, colorectal cancer and gastrointestinal oncology, microsatellite instability, IBD, acute hemorrhages in the gastrointestinal tract, capsule endoscopy, genetic screening, molecular mechanisms of carcinogenesis.

Scientific activity is evenly distributed over the years.

Teaching activity

Assoc. Prof. Mirchev had an annual load of seminars and lectures with the 5th year medical students - for the academic years from 2013/2014 to 2021/2022 up to 264 hours per year. He led seminars, gave thematic lectures, participated in the training of intern doctors, specialists and doctoral students.

Assoc. Prof. Mirchev is the supervisor of two doctoral students who are currently developing their dissertations - Dr. Alexander Yordanov and Dr. Alexander Trifonov.

Assoc. Prof. Mirchev leads the seminars for medical students from the 5th year of gastroenterology since 2012 and seminars for foreign medical students from the 5th course - since 2015. Assoc. Prof. Mirchev has excellent lecturing experience and is one of the main lecturers in English. He is a teacher respected and loved by the students. He actively participates in the development of educational materials for medical students and specialists in the field of internal medicine and gastroenterology, also in the overall process of internal medicine and gastroenterology training of medical students in Bulgarian and foreign language education, including intern doctors, by conducting practical exercises and seminars, and participation in examination committees for the final assessment of students on semester and state exams. He takes an active part in the training of specialized doctors at the Gastroenterology Clinic, including in the acquisition of a certificate for highly specialized activities in the field of gastrointestinal endoscopy.

Diagnostic and therapeutic activity

Dr. Mirchev for the first time thoroughly investigated the role of promoter methylation in the carcinogenesis of colorectal cancer. He was one of the pioneers in the introduction of capsule endoscopy in Bulgaria. He established himself as an experienced gastroenterologist and endoscopist. He has personal credit for introducing modern diagnostic and interventional methods into the clinic.

Assoc. Prof. Mirchev made an indisputable contribution to the introduction and validation of capsule endoscopy, interventional gastroscopy and colonoscopy, the use of NBI and magnifying endoscopy for screening. He was one of the main gastroenterologists-endoscopists serving UMBAL "St. Marina" for cases with acute bleeding from the gastrointestinal tract. He also presented a certificate of participation in the 24th International Endoscopy Symposium in Dusseldorf from February this year, credited with 13 European points.

Due to his extensive clinical experience and erudition, he participates in the Committee on the Treatment of Chronic Idiopathic Inflammatory Bowel Diseases, Chronic Viral Hepatitis and the Treatment of Patients with Wilson's Disease.

Assoc. Prof. Mirchev is an authoritative clinician and gastroenterologist with contributions in the field of modern gastroenterology, clinical genetics and gastrointestinal endoscopy. He enjoys a high reputation among his colleagues, students and patients.

Associate Professor Milko Mirchev is a highly intelligent clinical physician and scientist, with accurate judgement, extensive clinical and endoscopic experience. He knows all diagnostic and therapeutic methods, incl. upper and lower interventional endoscopy, abdominal ultrasound, methods of clinical genetics. He is a highly responsible doctor, sought after and respected by patients.

Assoc. Prof. Mirchev is an active member of BMU, the Bulgarian Society of Gastroenterology, EAGEN and ECCO. He is one of the main organizers of the national gastroenterology conferences, Gastroforum Varna and ECCO workshops in Bulgaria. He takes an active part in the conferences of the Bulgarian Scientific Society of Gastroenterology and international, national and regional scientific symposia and conferences. At the last congress of the Bulgarian Scientific Society of Gastroenterology in October of this year, he was elected a member of the Governing board of the society. He is a member of the Expert Council on Gastroenterology at the Ministry of Health of the Republic of Bulgaria. With his qualities, capabilities, knowledge and experience, he would be a source of pride for any European or global gastroenterology clinic and any Medical Faculty.

Assoc. Prof. Mirchev meets and exceeds the necessary minimum requirements according to the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Rules for its Application and the Rules for the Development of the Academic Staff at the University "Prof. Dr. Asen Zlatarov", Burgas. According to indicator A, he has 50 points, according to indicator B - 100 points, according to indicator D - 201 points, according to indicator D - 375 points, according to indicator E - 85 points, or in total - 811 points.

Conclusion

After detailed examination of presented scientific materials from the candidate, it can be concluded that Associate Professor Milko Bozhidarov Mirchev fully meets

the requirements for habilitation in the academic position "associate professor" in accordance with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Rules for its Application and the Rules for the Development of the Academic Staff composition at University "Prof. Dr. Asen Zlatarov", Burgas. Considering his scientific research activity, his pedagogical experience, publication and scientific activity, diagnostic and therapeutic activity and the contributions of the candidate, I propose to re-award the scientific title of "associate professor" to Assoc. Dr. Milko Bozhidarov Mirchev, MD.

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