

**ATTN: THE CHAIRMAN OF THE SCIENTIFIC JURY
AT THE MEDICAL UNIVERSITY “PROF. PARASKEV
STOYANOV” OF VARNA**

Concerning:

The participation of Krasimira Ivanova Koleva, MD, PhD in a competition announced in State gazette No 32/April 26, 2022 for tenure of the academic position of ‘**Associate Professor**’ in the field of higher education No 7 Public health and sports, professional trend No 7.1 Medicine and scientific speciality of **Pediatrics** - 0,5 pay-roll office for the needs of the Department of Pediatrics at the Faculty of Medicine of the Medical University ‘Prof. Paraskev Stoyanov’ of Varna and 0,5 pay-roll office for the needs the Second Pediatric Clinic at St. Marina University Hospital of Varna according to the Order No R-109-264/June 23, 2022, of the Rector of the Medical University ‘Prof. Paraskev Stoyanov’ of Varna, Valentin Lyubomirov Ignatov, MD, PhD.

PEER REVIEW

by

Prof. Nikola Yordanov Kolev, MD, PhD, DSc

*Department of General and Operative Surgery
Medical University ‘Prof. Paraskev Stoyanov’ of Varna
First Clinic of Surgery, St. Marina University Hospital of Varna*

According to Protocol No 67/June 20, 2022 of the Scientific jury appointed by Order of the Rector of the Medical University ‘Prof. Paraskev Stoyanov’ of Varna, Valentin Lyubomirov Ignatov, MD, PhD, I have been assigned to prepare the present peer review for the only candidate in the competition.

I. CONCISE BIOGRAPHIC AND PROFESSIONAL DATA

Krasimira Ivanova Koleva was born on June 17, 1966 in the village of Vetrino, Region of Varna. She graduated from the Medical University ‘Prof. Paraskev Stoyanov’ of Varna in 1999. Krasimira Koleva, MD, started to work as a physician in a medical centre. Since 2010, she was appointed as intern, and since 2017, she is assistant in the Department of Pediatrics at St. Marina University Hospital of Varna. During the period between 2019 and 2021, she is doctoral student in independent preparation form in the speciality of pediatric gastroenterology at the Department of Pediatrics. Krasimira Koleva, MD, acquires the educational and scientific degree of ‘doctor of philosophy’ in 2021. The theme of her dissertation work is ‘Some contemporary diagnostic aspects of inflammatory bowel diseases in children and adolescents’.

Specialities acquired

Krasimira Koleva, MD, has a recognized speciality of pediatrics in 2009 and a of pediatric gastroenterology in 2016.

II. EVALUATION OF CANDIDATE'S RESEARCH ACTIVITY

1. Scientometric indicators

Krasimira Koleva, MD, PhD, participates in the present competition with the following scientific works:

One dissertation work for the acquisition of the educational and scientific degree of 'doctor of philosophy'.

One-author monograph entitled 'Novelties in the treatment of ulcerative colitis and Crohn's disease in childhood and adolescence'.

A total of 29 full-text articles published in a total of eight Bulgarian journals and one foreign journal as the only or first author in seven articles (24,14%).

A total of six reports published in proceedings of five scientific forums in Bulgaria.

The total number of citations of her three articles is 11 (in seven articles by Bulgarian authors) and in four articles by foreign authors).

2. Participation in a research project

Krasimira Koleva, MD, PhD, is participant in one research project in the Medical University 'Prof. Paraskev Stoyanov' of Varna:

'Assessment of the expression levels of selected microRNAs as potential biomarkers in children and adolescents with inflammatory bowel diseases'.

III. MAIN RESEARCH TRENDS

The research activity of Krasimira Koleva, MD, PhD, is due to her intensive therapeutic and diagnostic work as authoritative pediatrician and pediatric gastroenterologist presenting with the children and adolescents with serious diseases of the gastrointestinal tract, liver, pancreas, etc.

The main trends in her research work are related to the modern diagnosis and treatment of the inflammatory bowel diseases, gastrointestinal and liver diseases in childhood and adolescence.

The novelties in the diagnosis of the inflammatory bowel diseases in childhood and adolescence have been systematized in the dissertation work and in the monograph while the recent scientific achievements and Dr. Krasimira Koleva's own experience in the field of the treatment of these socially significant diseases - in the monograph.

The diagnostic and differential-diagnostic value not only of several laboratory parameters such as erythrocyte and leukocyte count, concentrations of hemoglobin, serum iron, C-reactive protein, fibrinogen, fecal calprotectin, cytoplasmic and perinuclear antineutrophilic cytoplasmic antibodies) but also of modern methods for imaging diagnosis such as abdominal echography, computed tomography, fibrogastroduodenoscopy and

fibrocolonoscopy has been identified. Based on the own results and literature data, an original diagnostic algorithm concerning these diseases has been elaborated.

The features of cystic fibrosis, gastroesophageal reflux disease, primary and secondary gastroesophageal reflux in suckling age have been investigated. In a series of publications, the clinical symptoms, methods of diagnosis, genetic tests, complications and treatment of celiakia have been studied. The importance of gluten-free diet for the successful treatment of the disease, the role of DEXA and the place of osteocalcin and osteoprotegerin for the diagnosis of osteoporosis, one of the complications of celiakia, have been emphasized.

The issues of the intestinal flora and its relation to human health have been discussed. The important role of the intestinal and fecal microbiome for the human organism has been considered and the revolution of probiotics has been followed-up. The results from a single-centre prospective investigation with *Lactobacillus reuteri* DSM 17938 probiotic used for the prevention of the infections in children associated with the treatment with broad-spectrum antibiotics have been generalized.

Dr. Krasimira Koleva's publications devoted to the diseases in children in which chronic diarrhea is observed such as celiakia, cystic fibrosis, lactase deficiency, irritable bowel syndrome and inflammatory bowel diseases which cause nausea and vomiting represent an interest. The clinical picture of food allergy and, especially, of eosinophilic esophagitis, gastritis and gastroenteritis, atopic dermatitis, allergic proctocolitis, and contact dermatitis has been described.

In several articles, the diagnostic capacities for non-alcoholic fatty liver disease in childhood and adolescence have been investigated. The pathogenesis of the fatty liver degeneration with focus on this disease and its association with obstructive sleep apnea in children has been discussed.

The rare *vena portae* thrombosis related to kidney affection in children, adolescents and young persons, the deep venous thrombosis as a complication of ulcerative colitis in childhood and the deep venous thrombosis of the femoral and iliac veins in a child with acute ulcerative colitis have been reported. A kidney affection in children, adolescents and young persons with Wilson's disease and acute liver failure as a consequence of this disease has been described.

IV. MAIN ORIGINAL SCIENTIFIC CONTRIBUTIONS

The theoretical and applied contributions in the scientific works of Krasimira Koleva, MD, PhD, are in the following main thematic fields: pediatric gastroenterology, pediatric hepatology, pediatric pancreatology, clinical pediatrics, and intestinal microbiome. Several case reports deserve attention, too.

For the first time in Bulgaria, the additional differential-diagnostic role of 11 microribonucleic acids (microRNAs) in children with ulcerative colitis and Crohn's disease has been studied and statistically significant correlation dependences between microRNA195, microRNA131-a, microRNA142-3p, and microRNA223, on the one hand, and standard parameters of anemia and inflammation, on the other hand, have been revealed. For the first time in our country, the role of the microRNAs, serological tests and

elastography for the diagnosis of the non-alcoholic fatty liver disease in childhood and adolescence has been analyzed.

For the first time in Bulgaria, the constellation of appropriate contemporary laboratory and imaging methods of investigation in children and adolescents with Crohn's disease, ulcerative colitis and non-specific colitis has been defined.

pH-metry with impedance has been used during the diagnosis of the primary and secondary gastroesophageal reflux in suckling age for the first time in our country.

For the first time in Bulgaria, the experience with the application of the genetic tests for the predisposition to celiakia has been reported.

For the first time in our country, attention has been paid to malnutrition in the children with cystic fibrosis and advices for a correct nutrition within its correlation with the quality of life have been presented.

For the first time in our country, the scientometric aspects of the international scientific communications and dynamic institutionalization of research on the issues of Crohn's disease in children have been studied.

The publications devoted to suckling's nutrition, permeable alimentary tract, constipation, chronic liver disease and hepatorenal syndrome in childhood represent a definite contribution, too.

V. TEACHING, LECTURER'S AND PUBLIC ACTIVITY

Krasimira Koleva, MD, PhD, is involved in the education of medical students in the discipline of 'pediatrics'. Her teaching and lecturer's activity as assistant at 0,5 pay-roll office in the Department of Pediatrics during the period between 2017 and 2021 is the following: during the 2017-2018 academic year - 232 hours; during the 2018-2019 academic year - 210 hours; during the 2019-2020 academic year - 198 hours and during the 2020-2021 academic year - 216 hours.

Krasimira Koleva, MD, PhD, is member of several scientific societies and organizations:

1. Bulgarian Pediatric Association
2. Bulgarian Society of Human Genetics and Genomics
3. ESPGHAN (European Society of Pediatric Gastroenterology, Hepatology and Nutrition)
4. ECCO (European Crohn and Colitis Organization)

CONCLUSION

Based on the abovementioned facts I can declare that the professional qualification, research and teaching and lecturer's activity of Krasimira Ivanova Koleva, MD, PhD, completely meet the requirements of the Statute-book for the conditions and order for the acquisition of scientific degrees and for tenure of the academic position of 'Associate Professor' in the Medical University 'Prof. Paraskev Stoyanov' of Varna. That is why I recommend to the honoured members of the Scientific jury to vote positively for the tenure by Krasimira Ivanova Koleva, MD, PhD, of the academic position of 'Associate Professor'

in the Medical University 'Prof. Paraskev Stoyanov' of Varna for the needs of the Department of Pediatrics at the Faculty of Medicine of the Medical University 'Prof. Paraskev Stoyanov' of Varna and the Second Pediatric Clinic at St. Marina University Hospital of Varna.

Peer reviewer:

City of Varna
September 18, 2022

(Prof. Nikola Kolev, MD, PhD, DSc)