

REVIEW

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Subject: Competition for the academic position "Associate Professor" in the field of higher education 4. Natural Sciences, Mathematics, and Informatics, professional field 4.3. Biological Sciences, scientific specialty "Genetics," announced in the State Gazette issue 42/23.05.2025.

1. General presentation of the received materials

By order № ПД-269/23.07.2025 of the Rector of Burgas State University "Prof. Dr. Asen Zlatarov," on the grounds of Art. 57 (2) of the Regulations for the Development of Academic Staff in the Republic of Bulgaria, and Art. 70 (2) of the Regulations for the Terms and Conditions for the Acquisition of Academic Positions in the Burgas State University "Prof. Dr. Asen Zlatarov," in connection with the announced competition for the academic position "Associate Professor" in the field of higher education 4. Natural Sciences, Mathematics, and Informatics, professional field 4.3. Biological Sciences, scientific specialty "Genetics," and report with reg. № 2565/11.07.2025, I have been appointed as a member of the scientific jury for a competition for the academic position "Associate Professor" in the field of higher education 4. Natural Sciences, Mathematics, and Informatics, professional field 4.3. Biological Sciences, scientific specialty "Genetics," competition announced in State Gazette, issue 42/23.05.2025.

The only one candidate for the announced competition is Assistant Professor Miglena Antonova Koprinarova, PhD. She held the position Assistant Professor in the "Molecular Biology of the Cell Cycle" Department at the Institute of Molecular Biology, Bulgarian Academy of Sciences, from 2008 to 2021.

The documents submitted by Assis. Prof. Koprinarova are in accordance with the guidelines published in the Regulations for the Implementation of the Law on the Development of the Academic Staff in the Republic of Bulgaria and the requirements of the Regulations on the Terms and Conditions for Acquiring Scientific Degrees and Holding Academic Positions at Burgas State University "Prof. Dr. Asen Zlatarov".

The submitted documentation includes all required documents with all corresponding supporting materials.

As a member of this Committee, I declare that I have no joint publications, projects, or other conflicts of interest, as defined in Article 1, paragraphs 3 and 5 of the Law on the Development of the Academic Staff in the Republic of Bulgaria, with the candidate Assis.Prof. Miglena Antonova Koprinarova.

2. Brief biographical summary and evaluation of publication activity

Assis. Prof. Miglena Antonova Koprinarova completed her master's degree in "Cell and Developmental Biology" at the Faculty of Biology, Sofia University "St. Kliment Ohridski" in 1992. She obtained her PhD degree in 2008 from the Institute of Molecular Biology, Bulgarian Academy of Sciences and the title of her PhD thesis was: "Dynamics of Histone H4 Acetylation and Repair of Interstrand Crosslinks in the Cell Cycle." From 2008 to 2021 she was Assistant Professor in the "Molecular Biology of the Cell Cycle" Department at the Institute of Molecular Biology, Bulgarian Academy of Sciences. Over the years till now, the candidate has been actively involved in various national and international projects, supervised students, and participated in scientific forums. From 2020 to 2024, she was a part-time lecturer at the University of Food Technologies in Plovdiv, "Nutrigenomics" course. This demonstrates significant teaching experience, high qualifications, and skills with long-term potential for career growth.

3. Fulfillment of the Requirements for the Academic Position "Associate Professor"

The candidate has submitted a documents with detail information of the fulfillment of the national requirements based on the criteria groups outlined in the Law on the Development of the Academic Staff in the Republic of Bulgaria as well as the additional requirements for the "Associate Professor" position at Burgas State University "Prof. Dr. Asen Zlatarov".

Group A: The candidate presented the abstract of her dissertation titled "Dynamics of Histone H4 Acetylation and Repair of Interstrand Crosslinks in the Cell Cycle". This criteria gives a total score of 50 points.

Group B: The candidate submitted one monograph on the topic: "Butyrate, Gut Microbiome, and Nutrient-Mediated Modulations for Maintaining Homeostasis." This criteria gives a total score of 100 points.

Group G: The candidate presented 10 articles, which are peer-reviewed and indexed in globally recognized scientific databases, with total score of 184 points. Additionally, one book with gives a total score of 20 points. The total score for this group is 204 points, minimum required score was 200 points.

All 10 articles submitted in Group G are distributed as follows: one article in a Q1 journal, six articles in Q2 journals, one article in a Q3 journal, and two articles in Q4 journals. The candidate Assis. Prof. Koprinarova is the first author on five of these articles.

The candidate has submitted a total of 23 articles for this competition. Twelve of these are allocated to the Groups mentioned above, while the rest are in peer-reviewed scientific journals without an impact factor, popular science magazines, and articles in proceedings from scientific forums.

Group D reflects citations in peer-reviewed and indexed scientific databases (Web of Science and Scopus). According to Scopus, the candidate has 222 citations with an H-index 6 (source: <https://www.scopus.com/authid/detail.uri?authorId=23973145000#>). Assistant Professor Koprinarova has provided a list of 75 citations for the publications included in the competition, which gives a total score of 150 points. This significantly exceeds the required 50 points in the Law on the Development of the Academic Staff in the Republic of Bulgaria and the 100 points required by the Regulations on the Terms and Conditions for Acquiring Scientific Degrees and Holding Academic Positions at Burgas State University "Prof. Dr. Asen Zlatarov".

The publications and supplementary materials presented for this competition, with a total of 604 points, satisfy all the criteria required for the academic position "Associate Professor". The minimum required points is 400 by the Law on the Development of the Academic Staff in the Republic of Bulgaria and 550 points required by the Regulations of the Burgas State University "Prof. Dr. Asen Zlatarov". This demonstrates that Assis. Prof. Koprinarova is a highly productive and active researcher.

Group E shows evidence of the candidate's involvement as the leader of four national scientific projects funded by the Medical and Diagnostic Genetics Laboratory "Genika," and as a participant in two other projects funded by the Ministry of Education and Science's Scientific Research Fund. The total points for this group are 100, which exactly meets the requirements of the Law and Regulations of the university.

Group	Submitted Documents	Requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria	Requirements of the Regulations of Burgas State University "Prof. Dr. Asen Zlatarov" for "Associate Professor"	Points achieved by the candidate
A.	PhD Dissertation	50	50	50
B.	3. Habilitation work - monograph; or 4. Habilitation work - scientific publications in journals that are peer-reviewed and indexed in internationally recognized scientific databases (Web of Science & Scopus)	100	100	100
G.	6. Published book based on defended dissertation for obtaining "educational and scientific degree" "PhD" 7. Scientific publications in journals that are peer-reviewed and indexed in internationally recognized scientific databases (Web of Science & Scopus), excluding habilitation work	200	200	204
D.	11. Citations in scientific journals, monographs, collective volumes, and patents, peer-reviewed and indexed in internationally recognized scientific databases (Web of Science & Scopus)	50	100	150
E	14. Participation in a national scientific or educational project 16. Leadership of a national scientific or educational project	-	100	100
TOTAL		400	550	604

4. Main Research Directions and Contributions

The candidate's research activities and scientific contributions can be thematically grouped into the following main directions:

1. The Role of Butyrate in Maintaining Homeostasis and its Impact on Human Health

Butyrate is a short-chain fatty acid produced endogenously in the colon through microbial fermentation of dietary fibers, including those found in sourdough bread. It serves as a primary energy source for colon epithelial cells, maintaining mucosal integrity and preventing cellular death via autophagy in the absence of butyrate. The mechanisms of butyrate action are complex and include:

- a) **Inhibition of histone deacetylase (HDAC)**, leading to hyperacetylation of histone proteins and chromatin decondensation, thereby promoting gene expression.
- b) **Modulation of gene expression** via G-protein-coupled receptors.
- c) **Suppression of inflammatory processes** and reduction of oxidative stress.

d) **Regulation of the cell cycle** by stimulating the p21 gene and arresting cells in the G1 phase, subsequently inhibiting cell division, particularly in abnormal cells.

e) **Improvement of the intestinal barrier**, stimulation of transepithelial ion transport (e.g., NaCl), and regulation of peristalsis and neuronal communication between the enteric and central nervous systems.

Butyrate exhibits pleiotropic protective and therapeutic effects across a wide spectrum of diseases, including inflammatory bowel diseases, obesity, type 2 diabetes, cancer (colorectal carcinoma), cardiovascular diseases, and neurodegenerative disorders.

Contribution: A novel concept is formulated for the targeted stimulation of endogenous butyrate production through diet and microbiome intervention, demonstrating a proven effect on human health. A new concept regarding the role of endogenous butyrate production in maintaining homeostasis is presented. The link between sourdough bread consumption and the stimulation of butyrogenic bacteria in the colon is demonstrated, highlighting its beneficial impact on human health, including the prevention and treatment of inflammatory, metabolic, and oncological diseases.

2. Molecular Pathogenesis and Novel Therapeutic Approaches in Diseases

2.1. Spontaneous Abortions

Molecular changes in spontaneous abortions were investigated, revealing a high percentage (70%) of fetal genomic anomalies, predominantly numerical and structural aberrations. Particular attention was paid to the significantly increased expression of angiogenic factors VEGFA/VEGFR2 and chemokine systems SDF-1/CXCR4, indicating enhanced angiogenesis, which potentially contributes to pathogenesis.

Contribution: A novel characterization of the role of angiogenesis is proposed, which may serve as a basis for developing therapeutic strategies.

2.2. Epigenetic Response to NH₂-PS-NPs Nanoparticles

It has been demonstrated that these nanoparticles induce an epigenetic response by decreasing histone H3K9 acetylation levels. This leads to changes in gene expression, apoptosis, and cellular dysfunction, with a more pronounced impact on brain endothelial cells.

Contribution: The necessity of epigenetic monitoring of nanoparticles for safety assessment is emphasized.

2.3. Antitumor Activity of Aloe-Emodin

Mechanisms of cytotoxicity in human brain microvascular cells were elucidated, including the induction of Reactive Oxygen Species (ROS), disruption of mitochondrial membrane potential, and perturbation of calcium homeostasis. Studies indicate selective inhibition of cancer cell growth and relatively low toxicity towards normal endothelial cells.

Contribution: This research presents the potential for clinical application of Aloe-Emodin (AE) as a natural anti-angiogenic and antitumor agent.

2.4. Epigenetic Regulation of the Cell Cycle and Epigenetic Changes in Type 2 Diabetes

Details of histone H4 acetylation at different stages of the cell cycle were analyzed, demonstrating that this is a key mechanism for regulating progression and cell cycle arrest. Changes in DNA methylation in type 2 diabetes were analyzed, revealing a correlation between disease duration and the methylation status of genes associated with oxidative stress and tumor suppressors.

Contribution: This study contributes to understanding the epigenetic mechanisms in the progression of type 2 diabetes and suggests a possible role for these changes in disease complications, including increased oncological risk.

2.5. Epigenetic Sensitization of Tumor Cells through Sodium Butyrate and Irradiation

It has been demonstrated that butyrate enhances the response of tumor cells to radiation and cytotoxic agents by inhibiting DNA repair mechanisms and stimulating apoptosis.

Contribution: This research proposes a potential therapeutic strategy to increase the efficacy of radiotherapy and chemotherapy through combination with butyrate.

3. Microbiology and Biotechnology

3.1. Characterization of *Saccharomyces cerevisiae* Mutants

The selection of temperature-sensitive mutants that exhibit increased protein export, associated with active secretion, was investigated. At 38°C, these mutants display cell cycle delay and a series of structural changes, which are compensated by sorbitol addition. It was proven that this is an active process, dependent on ATP synthesis and occurring via a cell wall with increased porosity.

Contribution: Protein-exporting mutants with potential application in the biotechnology industry for the production of secretory proteins have been characterized.

5. Additional Activities – Participation in Scientific Projects, Scientific Forums, and Teaching

Assis. Prof. Koprinarova has more than 20 years of professional experience in Bulgaria and international settings, where demonstrated strong leadership and organizational skills. She is enable to work both independently and collaboratively, successfully providing guidance, training, and instruction to students and specialists. She has acquired a wide range of specializations and certified qualifications both in Bulgaria and abroad. In Bulgaria, she has completed numerous certified courses, making her exceptionally competent in the field of quality management systems according to ISO standards, including validation and accreditation of different methods. In molecular biology, she is proficient in techniques related to molecular-biological approaches and analyses crucial for the molecular diagnosis of respiratory and gastrointestinal diseases. All of this indicates a high degree of technical competence combined with laboratory management skills.

Her substantial accumulated experience and high qualifications in teaching will contribute to her development as an Associate Professor at the university. Her participation in national and international projects and conferences will foster new ideas for successful collaborations with Bulgarian and foreign teams and promote Burgas State University "Prof. Dr. Asen Zlatarov".

6. Critical Remarks and Recommendations

I have no critical remarks or recommendations regarding the candidate. All submitted documents have been prepared in accordance with the requirements.

7. Conclusion

The results achieved by the candidate fully satisfy the national requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria and the additional requirements of the Burgas State University "Prof. Dr. Asen Zlatarov" for the academic position "Associate Professor." Notably, the required points in the groups of criteria directly related to the quality of scientific output (Groups G and D) have been exceeded.

The candidate's work demonstrates original scientific and applied contributions that have received international recognition, with a representative portion published in peer-reviewed journals. The scientific qualification of Assist. Prof. Miglena Antonova Koprinarova is beyond doubt.

After reviewing the materials and scientific publications submitted for the competition, and analyzing their significance and inherent contributions, I'm satisfied and give my positive evaluation and recommend to the Scientific Jury to award Assistant Professor Miglena Antonova Koprinarova the academic position of "Associate Professor" in the field of higher education 4. Natural Sciences, Mathematics and Informatics, professional field 4.3. Biological Sciences, scientific specialty "Genetics," at the Burgas State University "Prof. Dr. Asen Zlatarov", Burgas.

20/09/2025

/Associate Professor Violeta Valcheva Ruseva, PhD /