REVIEW

for the competition for the academic position of **associate professor** in Higher Education Area 4. Natural Sciences, Mathematics, and Informatics, Professional Field 4.3. Biological Sciences (Scientific Specialty: Molecular Biology),

announced in the State Gazette, issue 104/10.12.2024,
for the needs of the "Molecular Biology of the Cell Cycle" section at the Institute of Molecular Biology "Acad. Rumen Tsanev," Bulgarian Academy of Sciences (IMB-BAS).

Reviewer: Prof. Dr. Galina Teneva Yahubyan
Scientific Specialty: Molecular Biology
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Appointed as a member of the scientific jury by order 32-OB/28.01.2025, IMB-BAS

The competition for the academic position of Associate Professor in Molecular Biology at IMB-BAS has one applicant: **Senior Assistant Professor Dr. Emil Damyanov Parvanov.**

The submitted documents comply with the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), its Implementing Regulations, and the Internal Regulations of IMB-BAS.

1. Candidate's Career Profile

Dr. E. Parvanov obtained a master's degree in molecular biology in 2001 from Sofia University "St. Kliment Ohridski." Even during his studies, he demonstrated a strong scientific interest in the structure and function of chromatin, developing and defending a master's thesis under the supervision of Assoc. Prof. Anastasia Bakalova (IMB-BAS).

His scientific career continued at the Institute of Cell Biology at the University of Bern, Switzerland, where he was awarded a Ph.D. degree in 2006 in Biological Sciences, specializing in yeast genetics.

Between 2007 and 2015, Dr. E. Parvanov conducted postdoctoral research at The Jackson Laboratory (Bar Harbor, USA) and Masaryk University (Brno, Czech Republic), focusing on projects related to mouse genetics. Later, between 2015 and 2021, he held the position of Research Associate at the Institute of Molecular Genetics, Czech Academy of Sciences (Prague, Czech Republic), where he further deepened his research in mouse genetics.

From 2021 to 2024, Dr. E. Parvanov worked as a researcher on an external project at the Medical University – Varna, focusing on optimizing the isolation of bone marrow stem cells. Since June 2024, he has held the position of Senior Assistant Professor at IMB-BAS.

2. Evaluation of the submitted report for compliance with the requirements with the Requirements of Article 26, Paragraph 1 of the LDASRB and the Criteria for Holding the Academic Position of Associate Professor (Appendix 1 of the Implementing Regulations of IMB-BAS).

In the current competition for the academic position of **Senior** Associate Professor, Senior Assistant Professor Dr. E. Parvanov is participating with the following scientific works:

- **Doctoral dissertation** – 50 points.

- **15 scientific publications**, published in peer-reviewed and indexed international journals, which do not overlap with the works submitted for the acquisition of the Doctoral degree. These include 9 research articles and 6 review articles. **5 publications are equivalent to a habilitation thesis,** classified under Group B indicators, earning the candidate 115 points, with Dr. Parvanov as the first author in three of them. 10 publications are classified under Group G indicators, earning the candidate 235 points.

The **quartile distribution** of all scientific publications submitted for the competition is as follows: 11 articles in Q1 (JCR IF), 3 articles in Q2 (JCR IF), 1 article in Q3 (JCR IF), **total JCR Impact Factor (IF): 122.18.**

The **scientific impact** of the candidate's work is documented by 1,057 citations of 32 scientific publications (according to the Web of Science and Scopus databases), contributing 2,114 points to the evaluation. The Hirsch index (h-index) is 15 (according to Scopus).

Dr. Parvanov has served as **principal investigator on two national projects** (40 points), attracting financial support for Masaryk University (Brno, Czech Republic) and the Institute of Molecular Genetics, Czech Academy of Sciences (Prague, Czech Republic) (178.4 points).

Senior Assistant Professor Dr. E. Parvanov has successfully **supervised one Ph.D. student** at Charles University (Prague, Czech Republic), with proof available in the university's digital repository (50 points).

The **scientific metric indicators** of Dr. Parvanov's research activities, with a total score of **2,782.4 points, far exceed the minimum criteria** for obtaining the academic title of Associate Professor, as per the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), its Implementing Regulations, and the Internal Regulations of the Institute of Molecular Biology – Bulgarian Academy of Sciences (IMB-BAS).

In accordance with the Regulations for Holding the Academic Position of Associate Professor at IMB-BAS, the candidate has submitted official documentation verifying 6 years and 4 months of work experience at the Institute of Molecular Genetics, Czech Academy of Sciences (Prague, Czech Republic).

3. Analysis of the main research areas of the candidate

Dr. E. Parvanov's long-standing research activities and interests can be categorized into two main areas, reflecting his contributions to both fundamental and applied science. The first area focuses on studying meiotic recombination—a key biological process essential for maintaining genetic diversity and evolutionary adaptation in eukaryotes. The second area addresses the growing need for innovative solutions in healthcare, encompassing digital health, patient safety, and personalized medicine.

3.1. Fundamental research on molecular mechanisms of meiotic recombination

Dr. E. Parvanov and his team investigate meiotic recombination in mice - a model organism widely used for studying gene function in mammals. Their research involves genetic crosses between two evolutionarily distant mouse strains: C57BL/6J and CAST/EiJ. One of their key experimental approaches is the creation of a congenic mouse line, where the telomere-proximal region of chromosome 1 is derived from CAST/EiJ, while the rest of the genome originates from

C57BL/6J. Hybrid offspring resulting from backcrossing this line with C57BL/6J are used to analyze recombination events in the heterozygous region of chromosome 1.

To track genetic variations, Dr. E. Parvanov employs single nucleotide polymorphisms (SNPs), which provide high precision in identifying recombination events. The high SNP frequency in the parental strains enables detailed mapping of genetic variations and analysis of recombination hotspot activity—regions in the genome with elevated recombination rates.

This experimental design offers a robust framework for uncovering the mechanisms governing meiotic recombination and identifying factors that shape genetic diversity in mammalian genomes.

- Mapping and characterizing meiotic recombination hotspots in mice

Dr. Parvanov conducts genotyping across the entire length of chromosome 1, coupled with sequencing of telomeric regions, allowing identification of recombination sites and hotspots (B4.1). One of his major findings is the uneven distribution of recombination activity across the chromosome—64% of DNA exhibits activity, while 36% remains inactive. Remarkably, nearly 50% of all recombination events are concentrated within only 7.6% of tested markers, suggesting approximately 40,000 recombination hotspots in the mouse genome.

The study also reveals differences in crossover interference between sexes. Crossover interference refers to the distance between two recombination events on the same chromosome. In females, this distance is shorter (measured in megabases), allowing more crossovers to occur simultaneously. As a result, female mice exhibit approximately 1.2 times more recombination events than males.

Additionally, the research identifies parental imprinting effects on recombination frequency, indicating complex regulatory mechanisms controlling meiotic recombination.

- Identifying and characterizing Prdm9 as an essential factor for recombination hotspot regulation

In search of genetic factors controlling recombination events, Dr. E. Parvanov uses QTL analysis to identify a regulatory region on chromosome 17 that activates recombination hotspots on chromosome 1 in CAST/EiJ mice (B4.2). Further genotyping and mapping narrow this region to 184 kilobases and lead to identifying Prdm9 as the factor responsible for hotspot positioning (B4.3).

Dr. Parvanov conducts a series of experiments to elucidate Prdm9's mechanisms of action (B4.4):

Functional Characterization: He experimentally confirms that Prdm9 determines hotspot positioning by directly binding specific DNA sequences.

Dual Methyltransferase Activity: Prdm9 encodes a histone methyltransferase with a zinc finger DNA-binding domain. In vivo studies show that Prdm9 trimethylates lysine 4 (H3K4me3) and lysine 36 (H3K36me3) on histone H3 upon binding to DNA. This unique combination is exclusively found at recombination hotspots, confirming its critical role in hotspot localization.

Correlation with Crossover Length: ChIP-seq analyses reveal a link between the number of nucleosomes marked by Prdm9 and crossover length, suggesting that Prdm9 not only marks recombination initiation sites but also regulates DNA exchange length during crossovers.

Genetic Diversity in Humans: Sequencing Prdm9 across human populations reveals significant allelic diversity, with the highest variability observed in African-American populations. The distribution of alleles aligns with established theories on human migration, highlighting Prdm9's evolutionary significance (B4.3).

Dr. E. Parvanov's findings significantly contribute to resolving the "hotspot paradox," which concerns the persistence of recombination hotspots over time (B4.3). The paradox arises due to gene conversion mechanisms—frequent use of a hotspot leads to its replacement by inactive sequences from homologous chromosomes, potentially depleting hotspots over time.

Dr. E. Parvanov demonstrates that high evolutionary variability in Prdm9's zinc finger domain creates new binding sites over time, ensuring the emergence of new hotspots and dynamically regulating meiotic recombination in the long term.

These results greatly enhance our understanding of meiotic recombination regulation, showing that Prdm9 not only determines hotspot positions but also controls DNA exchange extent during meiosis, providing a precise mechanism for generating genetic diversity.

3.2. Research in healthcare and medicine

- Traditional and Modern Approaches to Treating Liver Diseases

An important part of Dr. E. Parvanov's research interests is focused on liver diseases such as jaundice, alcohol abuse, and hepatocellular carcinoma. He has participated in extensive review studies aimed at integrating traditional medical practices with modern pharmacological approaches (G7.1, G7.2, G7.3, and G7.4). As a result of these studies, over 200 medicinal plants traditionally used to treat jaundice have been identified and documented. The research classifies these plants by family and reveals key active compounds such as silybin and andrographolide, which show significant potential in reducing bilirubin levels and normalizing liver function.

Dr. Parvanov has also contributed to studies on the therapeutic potential of plants like *Pueraria lobata* and *Hypericum perforatum* in the context of alcohol abuse. Special attention is given to bioactive compounds that modulate metabolic pathways associated with alcohol consumption, highlighting the potential of natural products as safer alternatives to conventional treatments.

Additionally, he has participated in a systematic review of available studies on NRF2—a key transcription factor involved in redox homeostasis. The analysis provides valuable insights into NRF2's dual role in liver health: while its activation protects against oxidative stress, aberrant activation due to mutations can accelerate the development of hepatocellular carcinoma.

- Bibliometric Studies on Health Misinformation and Public Reactions During the COVID-19 Pandemic

Dr. E. Parvanov has been involved in bibliometric analyses of misinformation on social media during the COVID-19 pandemic (G7.5). An analysis of 529 articles from Web of Science reveals an uneven focus on major platforms (Twitter, YouTube, Facebook) and the dominance of U.S.-based research. The study emphasizes the need for global collaboration and innovative methods such as machine learning to combat health misinformation, especially during crises.

A bibliometric analysis of 1,000 publications on rapid antigen tests for COVID-19 confirms their critical role in pandemic management across various settings—emergency departments,

healthcare facilities, airports, and workplaces (G7.7). The analysis highlights gaps in understanding their effectiveness for asymptomatic transmission and in post-pandemic contexts.

Using data from Google Trends, Dr. Parvanov and his colleagues examined interest in different types of masks in the ten countries with the highest COVID-19 cases (G7.9). They found that search interest peaked before mandatory measures were introduced and correlated with the stringency of government policies but not with virus transmission rates.

Dr. Parvanov's research contributes to understanding information behavior, the effectiveness of diagnostic strategies, and the dynamics of public reactions during health crises.

- Bibliometric Studies on the Application of Digital Technologies in Medicine

Dr. E. Parvanov's achievements focus on developing and applying digital health technologies in cardiology, blood pressure monitoring, and diabetes management (G7.6, G7.8, G7.10). His research highlights the growing role of smartphone applications and wearable devices for cardiovascular health, the increasing adoption of non-invasive sensors for continuous blood pressure monitoring, and advancements in continuous glucose monitoring systems.

His work emphasizes integrating digital tools into medical practice to improve patient monitoring, diagnostics, and chronic disease management. These studies provide an in-depth perspective on contemporary trends in medicine by combining traditional and digital approaches to enhance diagnostics, treatment, and patient safety.

4. Personal contribution of the candidate and significance of his achievements for science and society

All scientific publications by Assistant Professor Dr. E. Parvanov have been co-authored. His individual contribution to each scientific project is clearly described in the candidate's documents, including the section Author Contributions for each publication. Based on this, it can be concluded that the candidate played an active role in planning, execution, and securing funding, particularly evident in projects related to elucidating the molecular mechanisms and determinants of meiotic recombination.

In response to current challenges in public health, Dr. E. Parvanov's scientific interests have undergone significant development. He has made substantial contributions to applied research aimed at addressing modern health challenges, including the COVID-19 pandemic and digital health innovations.

The results of his research have been published in some of the most prestigious international journals. Among these, a notable publication in Science (2010) with a JCR IF of 47.73 stands out: Parvanov ED, Petkov PM, Paigen K. Prdm9 controls activation of mammalian recombination hotspots, where Dr. E. Parvanov is the first author. His publications have garnered significant scientific recognition, as evidenced by their citation count.

In summary, Dr. E. Parvanov's work focuses on key issues such as genetic diversity, digitalization of healthcare, and public health crises, while simultaneously providing direct benefits to patients and healthcare professionals. His achievements illustrate the successful integration of fundamental scientific discoveries with practical applications, contributing both to the advancement of scientific knowledge and societal well-being.

5. Critical notes and recommendations

The scientific works and activities presented by Assistant Professor Dr. E. Parvanov meet the scientific specialty of the competition in terms of both volume and quality, and I have no critical remarks about them.

CONCLUSION

The scientific output of Senior Assistant Professor Dr. E. Parvanov contains significant scientific and applied scientific contributions, which are visible to the international scientific community. Based on the presented competition materials, his growth as a researcher with in-depth knowledge and methodological skills in a number of areas of molecular genetics and cell biology is evident, as well as a creative and correct partner in joint research projects. Dr. E. Parvanov possesses knowledge and skills that constitute a valuable resource for the implementation of innovative scientific methodologies, the development of sustainable international partnerships, and the training of young researchers at the IMB–BAS, as well as for strengthening the global standing of Bulgarian science.

The candidate, Senior Assistant Professor Dr. E. Parvanov, meets the mandatory and specific conditions and scientific-metric criteria for the academic position of "associate professor" according to the requirements of the Law for the Development of Academic Staff in the Republic of Bulgaria, the Regulations for its implementation, and the Regulations of the Institute of Molecular Biology, Bulgarian Academy of Sciences (IMB, BAS). I confidently give my **positive assessment** of the academic presentation of Senior Assistant Professor Dr. E. Parvanov in this competition. **I recommend that the Scientific Jury prepare a report-proposal to the Scientific Council of IMB, BAS, for the election of Senior Assistant Professor Dr. Emil Damyanov Parvanov to the academic position of "associate professor" at IMB-BAS, in the field of higher education 4. Natural sciences, mathematics and computer science, professional field 4.3. Biological Sciences (scientific specialty Molecular Biology).**

Reviewer: Prof. Dr. Galina Teneva Yahubyan
Date: April 07, 2025