ASSESSMENT REPORT

by Prof. Dr. Valya Nikolova Vassileva, Institute of Plant Physiology and Genetics, Bulgarian Academy of Sciences

for a competition for the academic position "Associate Professor", *Field of higher education*: 4. Natural Sciences, Mathematics and Informatics; *Professional field*: 4.3 Biological Sciences; *Scientific specialty*: "Molecular Biology" at the Institute of Molecular Biology "Acad. Roumen Tsanev", Bulgarian Academy of Sciences

1. General information about the competition and submitted documents

The competition for the academic position of Associate Professor was announced in issue 104 of the State Gazette on December 10, 2024, for the needs of the "Molecular Biology of the Cell Cycle" section of the "Acad. Roumen Tsanev" Institute of Molecular Biology (IMB), Bulgarian Academy of Sciences (BAS). One candidate, Dr. **Emil Damyanov Parvanov**, Assistant Professor at IMB, has submitted an application.

The submitted materials comply with the requirements of the Act for the Development of the Academic Staff in the Republic of Bulgaria (ADASRB), the Regulations for the Implementation of the ADASRB, and the Rules on the acquisition of academic degrees and academic positions at BAS and IMB.

The research of Dr. Parvanov is of substantial volume and quality, and its thematic focus fully aligns with the profile of the announced competition. All required documents have been submitted, including a CV, a copy of the PhD diploma, certificates of professional experience, a list of publications submitted for the competition, a statement of compliance with the minimum national requirements for the academic position of *Associate Professor*, a report on scientific contributions, abstracts and copies of the publications, and a summary of scientific achievements. These materials provide a solid basis for an objective assessment of the Candidate research and training activities.

2. Information about the professional development of the Candidate

Assistant Professor Dr. Emil Parvanov obtained his Master degree in Molecular Biology with a specialization in Biochemistry from Sofia University "St. Kliment Ohridski" in 2001. In 2006, he defended his PhD thesis at the University of Bern (Switzerland), where he investigated meiotic recombination in *Schizosaccharomyces pombe* and revealed a novel epigenetic regulatory mechanism through a chromatin-dependent process involving the Swi5 protein, as well as the influence of cell type on gene conversion frequency.

The professional career of Dr. Parvanov includes extensive international research experience as a postdoctoral fellow and researcher at The Jackson Laboratory (USA), Masaryk University (Brno, Czech Republic), and the Institute of Molecular Genetics of the Czech Academy of Sciences (Prague, Czech Republic). From 2021 to 2024, he participated in an external research project at the Medical University of Varna, where he worked on translational biology of stem cells. Since June 2024, he has held the position of Assistant Professor at IMB-BAS. This consistent research activity demonstrates the progressive development of the academic career of Dr. Parvanov in thematic areas that fully align with the profile of the announced competition.

3. Overview of research activity of the Candidate

3.1. Fundamental and applied research activity

For participation in the competition for the academic position of Associate Professor, Dr. Emil Parvanov has presented 15 research papers with a total impact factor of 122.18, including three publications in which he is the first author. The high quality of his scientific output is evident - 12 articles have been published in first-quartile (Q1) journals, and the remainder in Q2 and Q3 journals. Among them are publications in prestigious international journals such as *Science*, *PLoS Biology*, *PLoS Genetics*, *Molecular Biology of the Cell*, *Frontiers in Pharmacology*, *Journal of Medical Internet Research*, *International Journal of Molecular Sciences*, and others.

The research of Dr. Parvanov demonstrates clear thematic focus and makes major contributions to several advanced scientific fields, including meiotic recombination and epigenetic regulation in mammals, chromatin biology, digital medicine and pharmacology. These findings have applications in understanding the molecular mechanisms underlying genetic variability and infertility, and in the development of analytical tools for the processing and interpretation of health and scientific information in the digital era. The Candidate is a co-author

of a total of 32 scientific publications, has participated in over 20 international conferences, and actively contributes as a reviewer for respected peer-reviewed journals.

3.2. Compliance with the minimum national and institutional requirements for the academic position of Associate Professor

The materials submitted by Dr. Parvanov meet, and in several respects greatly exceed, the minimum national requirements and the specific criteria of BAS and IMB for appointment to the academic position of Associate Professor, as follows:

Group A: Successfully defended PhD thesis in the professional field: 4.3 Biological Sciences – **50 points** (minimum required: 50 points).

Group B: Five scientific publications earning a total of **115 points** (minimum required: 100 points), including four in Q1 journals (*Science*, *PLoS Biology* and *PLoS Genetics*) and one in a Q3 journal (15 points).

Group C: Ten publications earning **235 points** (minimum required: 220 points), of which seven are in Q1 journals (175 points) and three in Q2 (60 points).

Group D: A total of 1057 citations in Web of Science/Scopus, amounting to **2114 points** (2 points per citation), far exceeding the required 60 points and demonstrating the Candidate strong international visibility and the considerable impact of his research contributions.

Group E: Although this group has no fixed threshold, it plays an important role in the comprehensive evaluation of the Candidate. Dr. Parvanov accumulates **268.4 points** based on the supervision of a successfully defended PhD student (50 points), leadership of two research projects (40 points), and securing external funding exceeding BGN 890 000 (178.4 points). This clearly reflects his active engagement in research, project development and scientific management.

The total number of accumulated points is **2782.4**, compared to the minimum of 400 points required by national regulations (ADASRB), and 430 points as set by the internal rules of BAS and IMB. The materials presented by Assistant Professor Dr. Emil Parvanov not only meet, but in several categories substantially exceed the required thresholds. His scientific output is distinguished by its high quality, international recognition and meaningful contributions to the development of molecular biology and its applied fields.

3.3. Scientific contributions of the Candidate

The scientific contributions of Dr. Emil Parvanov can be grouped into four interrelated research areas, reflecting both his foundational work in meiotic recombination and his more recent studies in the field of digital health and personalized medicine.

3.3.1. Mapping of meiotic recombination events in mammals

Through the analysis of over 6000 meiotic events, genotyped across the entire chromosome 1 in mice, the most detailed map of recombination events in mammals to date has been constructed. It has been established that 90% of crossovers are concentrated in 10% of genomic intervals, with approximately half occurring in just 7.6% of the chromosome. Thousands of recombination hotspots with uneven activity have been identified, forming distinct "hot" and "cold" zones. Considerable sex differences in recombination patterns have been observed - in females, the frequency of crossovers is approximately 1.2 times higher due to structural differences in the synaptonemal complex and the degree of chromosome compaction. Differences in interference between sexes have also been described, as well as the independent behavior of gene conversions relative to crossovers. The results provide valuable information on the regulation of meiotic recombination and its relationship to genetic variability, infertility and chromosomal abnormalities (*publication B4.1*).

3.3.2. Discovery and characterization of trans-acting factors determining the activity and position of recombination hotspots

Through QTL analysis, a genetic locus on chromosome 17, designated Rcr1, has been identified as controlling the activity and positioning of recombination hotspots on chromosome 1 (*publication B4.2*). The absence of CAST alleles in the rest of the genome leads to the disappearance of existing hotspots and the emergence of new ones, providing evidence for the presence of trans-acting factors. It has been shown that Rcr1 regulates both crossovers and gene conversions, likely by affecting the sites of DNA double-strand breaks. Further

mapping narrowed the locus down to 181 kb and led to the identification of the *Prdm9* gene as a main regulator of the recombination landscape in mammals (*publication B4.3*). *Prdm9* encodes a histone methyltransferase with highly variable zinc fingers that recognize specific DNA sequences and determine the locations of recombination events. The high allelic variability of *Prdm9* explains the hotspot distribution in different mouse lines and provides an explanation for the so-called "hotspot paradox", a phenomenon associated with the evolutionary disappearance of active recombination sites.

3.3.3. Elucidation of the molecular mechanism of *Prdm9* action

Dr. Parvanov has demonstrated that Prdm9 functions as a histone methyltransferase, simultaneously trimethylating H3K4 and H3K36 on nucleosomes at recombination hotspot regions. These dual histone modifications are specific to active recombination sites and correlate with the length of resulting crossovers (*publication B4.4*). In vitro analyses showed that both modifications can be placed on the same nucleosome with the methylation kinetics of H3K36 being considerably slower than that of H3K4. Using yeast two-hybrid screening and co-immunoprecipitation, Prdm9 protein partner have been identified – CXXC1, EWSR1, EHMT2, and CDYL, which interact via the KRAB domain *(publication B4.5*). Interactions with proteins from the meiotic cohesion and synaptonemal complex, REC8, SYCP1 and SYCP3, have also been confirmed. Based on these data, a model has been proposed in which Prdm9 recognizes specific DNA sequences in chromatin loops through its zinc fingers, trimethylates adjacent nucleosomes, and through protein interactions ensures the targeting of recombination sites to the chromosomal axis. This creates a favorable environment for the initiation of double-strand breaks by the SPO11 complex and subsequent meiotic recombination. These results provide a comprehensive mechanistic model for the role of Prdm9 as a central coordinator of the molecular events leading to the initiation of meiotic recombination in mammals.

3.3.4. Analysis of trends in digital health, patient safety and personalized medicine

The Candidate has made valuable contributions to bibliometric and review studies related to contemporary aspects of digital medicine and personalized healthcare. The first research area focuses on the application of plant-derived compounds in liver diseases such as jaundice, alcohol-induced damage and hepatocellular carcinoma. These publications examine bioactive plant compounds, their mechanisms of action and therapeutic potential with lower toxicity (*publications G7.1–G7.4*). The second area includes analysis of social and informational aspects of healthcare during the COVID-19 pandemic, such as misinformation on social media, public attitudes toward antigen tests and the use of protective face masks (*publications G7.5, G7.7, G7.9*). The third area is dedicated to digital innovations in medicine with an emphasis on patent and bibliometric analyses of non-invasive sensors for monitoring of blood pressure and glucose levels, as well as technological solutions in cardiology. Over 12,000 scientific publications and dozens of patent files have been analyzed to identify leading technologies, manufacturers and countries (*publications G7.6, G7.8, G7.10*). These interdisciplinary contributions demonstrate the analytical capacity of the Candidate and his capacity in advancing sustainable and technology-informed healthcare.

The Candidate has formulated broadly **scientific perspectives** focused on the investigation of the role of histone variants and chromatin modifications in the transitions of cells between different functional states and the development of diseases. The proposed directions have the potential to contribute to fundamental research and to the development of therapeutic approaches targeting epigenetic mechanisms.

4. Project leadership and research management

Dr. Emil Parvanov has established experience in leading and managing scientific projects with international funding, e.g., South Moravian grant co-financed by the Marie Curie program, and a project by the Czech Science Foundation (GACR). He has led research related to Prdm9, histone modifications and meiotic recombination, taking responsibilities for preparation of project proposals, and scientific coordination and administration of international projects.

5. Training activities

Dr. Parvanov has experience in academic training as a supervisor of a doctoral student at Charles University in Prague, Czech Republic. Additionally, he has participated in conducting laboratory exercises for students

through which he has acquired training skills. This experience provides a solid foundation for future expansion of his teaching activities in the academic community.

6. CRITICAL REMARKS AND RECOMMENDATIONS

I have no major critical remarks, except for a few noted technical inaccuracies. For example: i) the use of Cyrillic script for gene names („Прдм9" in the CV) may lead to misunderstandings; ii) the submitted materials include a list of 15 publications, while Section II states that there are 13 articles; iii) the list of publications lacks the labels B4.4, B4.5 and G7.10, although these are present in the "Summary of scientific contributions" and are cited as specific research results under the relevant thematic areas.

It is advisable for the Candidate to strengthen his leading role as first or corresponding author in future publications, particularly in fields such as digital medicine, where he has already demonstrated interdisciplinary potential. It would be helpful to outline a long-term research program that brings together his experience in chromatin structure and histone variants, and guides his future work toward uncovering the mechanisms by which they influence cell states and disease. This would further strengthen the strategic focus and sustainability of his future research.

CONCLUSION

Dr. Emil Damyanov Parvanov presents a rich and convincing academic biography that combines fundamental research in the field of meiotic recombination and epigenetic regulation with interdisciplinary studies in digital healthcare and personalized medicine. Dr. Parvanov possesses extensive international experience in prestigious research institutions and active involvement in research projects. His scientific output is of high quality and widely cited, demonstrating its strong international visibility and recognition in the academic community. The submitted materials fully meet, and in some aspects, greatly exceed the national and institutional minimum requirements for the academic position of Associate Professor. The research interests of Dr. Parvanov align closely with the thematic profile of the "Molecular Biology of the Cell Cycle" section, and demonstrate strong potential for the development of innovative and competitive scientific activity.

Based on the above, I recommend that the members of the esteemed Scientific Jury propose to the Scientific Council of IMB-BAS to appoint Dr. Emil Damyanov Parvanov to the academic position of Associate Professor in the professional field 4.3. Biological Sciences, scientific specialty "Molecular Biology".

April 22, 2025
Sofia

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