Институт по молекулярна биология - БАН
Вх. № 77-РД
Година, 25.04.25

REVIEW

Subject: Competition for the academic position of *Associate Professor* at the Roumen Tsanev Institute of Molecular Biology at the Bulgarian Academy of Sciences (IMB-BAS)

Reviewer: Prof. Roumyana Silvieva Mironova, PhD, IMB-BAS

By Order No. 32-OB/28.01.2025 of the Director of IMB-BAS I have been appointed as a member of the Scientific Jury in a competition for 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 of ***Molecular Biology*** for the needs of the **Molecular Biology of the Cell Cycle** Department at the IMB-BAS, according to an advertisement in the State Gazette, issue 104/10.12.2024. Only one candidate, Dr. Emil Damyanov Parvanov, Assistant Professor at the same institution, has submitted documents for the competition. The documents submitted to me on paper and in electronic format for participation in this competition comply with the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB) and the Regulations for its implementation (amended and supplemented by State Gazette No. 15 of 19.02.2019), as well as with the specific requirements of the Regulations on the Development of the Academic Staff at the Bulgarian Academy of Sciences and the IMB-BAS. The candidate has submitted a reference of work experience at the Institute of Molecular Genetics of the Czech Academy of Sciences, amounting to 5 years, 8 months and 20 days, which makes him legitimate for participation in the competition, although his total work experience in the field of Molecular Biology is much greater (evident below from his biographical data), for which, however, no certificates from the relevant institutions have been provided.

Biographical data

Dr. Parvanov graduated from the Faculty of Biology of Sofia University St. Kliment Ohridski in 2001 with a Master's degree in Molecular Biology with specialization in Biochemistry, which shows that his university education fully corresponds to the Molecular Biology specialty of the announced competition. The candidate obtained his PhD in 2006 with the topic of his doctoral thesis "The mating-type related bias of gene conversion at *ura4A* hot spot in *Schizosaccharomyces pombe*" under the supervision of Prof. Dr. Jürg Kohli from the Institute of Cell Biology of the University of Bern (Switzerland). After obtaining his Ph.D., between 2007 and 2014, Dr. Parvanov carried out two post-doctoral studies in succession, the first in the field of mouse genetics at the Jackson Laboratory in the USA, and the second in the field of biochemical analysis of proteins involved in DNA repair at Masaryk University (Brno, Czech Republic). Upon completion of both post-doctoral fellowships, the candidate returned to the Jackson Laboratory, where he worked as a scientist until 2015, and from 2015 to 2021 he held the same position at the Institute of Molecular Genetics of the Czech Academy of Sciences (Prague, Czech Republic). His research as a scientist in this period was exclusively in the field of mouse genetics. Specifically, he conducted research with proteins involved in DNA recombination, as well as studies on the genetics of hybrid sterility. In 2021, Dr. Parvanov returned to Bulgaria, where he was working as a researcher on an external project in the field of translational stem cell biology at the Medical University of Varna. *These brief biographical data reveal a focused professional and career development of the candidate with accumulated*

extensive research and methodological experience in the Molecular Biology specialty of the announced competition, also including research activities in prestigious scientific institutions abroad.

Scientific metrics

In relation with the PhD degree, Dr. Parvanov has published one article, which is excluded from the list of his publications for participation in the current competition and is therefore no subject of a peer review. In the announced competition of Associate Professor he participates with a total of 15 articles refereed in Web of Science, the majority of which (11 or 73%) fall into the category with the highest quartile Q1. Three of the remaining articles are Q2 and one is Q3. The overall JCR-IF of all the candidate's publications is very high at 122.18. In this regard, I note that one of the papers, concerning mechanisms of recombination in mammals, was published in the prestigious journal Science (IF 47.73). In three of the publications, including the one published in Science, Dr. Parvanov is first author. The articles with which Dr. Parvanov participates in the current competition have been cited many times, a total of 1057 times, which exceeds 35 times the minimum required for this position, according to the regulations for the implementation of LDASRB at BAS. *The high impact factor of the publications with which Dr. Parvanov participates in the current competition and their citation more than a thousand times, is indicative of the high level of his scientific production and its wide resonance among the international scientific community.*

Research areas and contributions

The scientific works submitted by the applicant in this competition can be divided into two main categories, which correspond to the two main groups of indicators (B and G) of the table on the compliance of the applicant's assets with the minimum national requirements under the LDASRB.

The first category comprises publications equivalent to a habilitation thesis (group B) and includes a total of five articles (**B4.1-B4.5**). A habilitation thesis implies that the research presented in it is monolithic in nature and is united by a common theme. In this case this requirement is strictly fulfilled and the five publications are devoted to the interesting topic of recombination mechanisms. The DNA recombination processes are crucial for maintaining the integrity of the genome and its variability. We can tentatively distinguish two important roles of DNA recombination, in meiosis and in DNA repair. Dr. Parvanov's habilitation thesis focused entirely on DNA recombination during meiotic division of mating cells. At the time he began his research, it was well known that there are both preferred and avoided sites for genetic exchange (recombination) along homologous chromosomes. However, up to this point, it was not clear what *cis*- and *trans*-acting factors underlie this specificity of homologous recombination in all organisms. This fact specifies the significant scientific contribution of Dr. Parvanov's research in this field. By using appropriate mouse genetic lines in publication **B4.1**, concerning *cis*-acting factors in recombination, it is shown that 1) the majority of the recombination events are concentrated in a small region of chromosome 1; 2) recombination activity is distributed unevenly along the chromosome; and 3) regions longer than 1,500 kb with no genes generally do not undergo recombination. Other interesting observations described in this publication include 1) the phenomenon of crossover interference, which only applies to reciprocal exchange processes (crossing over) but not to nonreciprocal exchange (gene conversion); 2) sex-dependent specificity of crossing over interference, which results in 1. 2-fold more recombination events in

females; and 3) significantly longer (up to 20-fold) DNA regions where crossing over has occurred compared to gene conversion regions.

Publications **B4.2 - B4.5** refer to trans-acting factors in the meiotic recombination. A successful model for genotyping and mapping of meiotic recombination events along chromosome 1 has been established by appropriate crosses of two mouse cell lines. Thus, the interesting observation was made that activation and repression of recombination hotspots in both sexes is allele-specific and due to a gene located on chromosome 17 (**B4.2**). Further studies have shown that this is a known gene (*Prdm9*) that encodes a histone methyltransferase (**B4.3**). The known structure of the protein encoded by this gene provides a good and logical explanation for a scientific problem long known as the "hotspot paradox". The outstanding scientific contribution of this study, in which Dr. Parvanov is the first author, is evidenced by the fact that it was published in Science, one of the journals with highest reputation among scientists.

The contributions in publications **B4.4** and **B4.5** relate to the discovery of the mechanism of action of the PRDM9 protein. Of scientific merit are the studies showing that this well-known methylase trimethylates not only histone 3 lysine 4 but also lysine 36 and that PRDM9 not only indicates where recombination will be initiated but also specifies how long the exchanged DNA will be when crossover occurs (**B4.4**). A combination of *in vitro* experiments, yeast two-hybrid assay, and co-immunoprecipitation of mouse spermatocytes further demonstrate that PRDM9 *via* the KRAB domain interacts with other histone modifiers, meiotic cohesins, and the synaptonemal complex. An interesting model (**B4.5**) has been established for the mechanism of action of PRDM9 involving its synthesis, specific binding to DNA, manifestation of its enzymatic activity and interaction with other proteins. All this identifies PRDM9 as the first master regulator of meiotic DNA recombination discovered in mammals, a scientific contribution of the greatest weight in the candidate's publications. *All of the candidate's publications, equaling to a habilitation thesis with significant contributions, are entirely in the field of Molecular Biology and devoted to fundamental scientific problems.*

The second area of the candidate's research (publications from G indicator group) concerns the analysis of trends in digital healthcare, patient safety and personalized medicine. Some of the articles summarize information on the action of different herbal substances in the treatment of liver diseases such as jaundice (**G7.1** and **G7.2**); diseases caused by alcohol intake (**G7.3**) and include also a review on the molecular mechanisms leading to the development of hepatocellular carcinoma (**G7.4**). Another part of Dr. Parvanov's research in this field consists of bibliometric analyses concerning the use of rapid immunological tests (**G7.7**), the use of different types of protective masks (**G7.9**), and the dissemination of false medical and health information during the COVID-19 pandemic (**G7.5**). A third subset of articles is devoted to the application of digital technologies in cardiology (**G7.6**), non-invasive sensors for blood pressure monitoring (**G7.8**) and for determining blood glucose levels (**G7.10**). *This group of publications is indicative of Dr. Parvanov's experience in handling large sets of digital information, which will be useful in his future research activities.*

Teaching and Project Activities

In the period from 2017 to 2022, Dr. Parvanov was the main supervisor of one PhD student, Amisa Mukaj, at Charles University (Prague, Czech Republic). In the period from 2011 to 2020, he was the PI of two research projects. One of them on "*Prdm9* - linking histone modifications and DNA recombination" was funded by the South Moravian Fund (SoMoPro) with co-funding from the Marie Curie Foundation, and the second project "Role of *Prdm9* alleles

in mouse hybrid sterility" was implemented with financial support from the Czech Science Foundation (GACR). For implementation of these two projects, the applicant has recruited funds equaling to BGN 892,434.49. *The two projects are in the field with the most significant scientific contributions of the applicant, which is indicative of his ability to financially support the realization of his scientific interests and research.*

Compliance with the requirements of LDASRB, BAS and IMB-BAS

The following table presents the compliance of the group of indicators A to F of Dr. Parvanov with the national minimum scientometric requirements, according to Table 1 of the Regulations for the implementation of LDASRB (adjusted for BAS/IMB at indicators G and D):

Indicators' Group	**Minimum number of points**	**Candidate's points**
A	50	50
B	100	115
G	200 (220 for BAS)	235
D	50 (60 for BAS)	2114
E	not required	268.4
Total	**430**	**2782.4**

The table shows that the candidate's assets significantly exceed the minimum national requirements for all indicators. Particularly impressive are his citation scores, which exceed the required minimum by 35 times, as well as his scores for indicator E, reflecting his leadership role in the training of a doctoral student and in attracting funds. Note that activities in indicator E are not required for the academic position of Associate Professor.

CONCLUSION

The analysis of the documents submitted by Dr. Parvanov shows that he possesses the required competencies in the field of Molecular Biology to occupy the position of Associate Professor under this competition. His scientometric indicators cover and exceed more than six times the requirements of LDASRB, the Regulations for its implementation and the Regulations of BAS and IMB-BAS. The candidate's scientific works contain original scientific contributions with significant scientific and applied potential. These studies have been published in renowned international journals (including *Science*) and have been cited over a thousand times to date. Dr. Parvanov has also gained invaluable experience in supervising doctoral students and in managing research projects, which is a good prerequisite for a successful occupation of the new academic position. All this gives me reason to confidently recommend to the Scientific Council of IMB-BAS to elect Assist. Prof. Emil Damyanov Parvanov, PhD, to the academic position of Associate Professor in Molecular Biology.

April 24, 2025

Prof. R. Mironova