



OPINION

by Dr. Anastas Dimitrov Pashov, Associate Professor at the Institute of Microbiology - BAS

according to Order No. 110-OB/28.06.2024 of the Director of the Institute of Molecular Biology "Academician Rumen Tsanev" at BAS (IMB-BAS) for the procedure for the defense of a dissertation for the award of the scientific degree "Doctor of Sciences" in the professional field 4.3 "Biological Sciences"

Author: Professor Dr. STEFAN IVANOV DIMITROV

Topic: CHROMATIN - FROM STRUCTURE TO FUNCTION

Professor Stefan Dimitrov is an established scientist with many years of research activity in various institutions abroad. He has led a highly productive scientific team at the University of Grenoble, France for over 15 years. His main contributions are in the study of chromatin and histone variants.

DNA is organized into hierarchical chromatin structures with varying degrees of compaction, and key biological processes in the cell occur in this context. Understanding the mechanisms behind this packaging and the role of epigenetic factors, in particular through histone variants, is key to elucidating DNA functions and their relationship to various pathological processes.

Prof. Dimitrov's research significantly expands the understanding of the structure and function of chromatin, especially the role of histone variants and high-level chromatin organization. His group has investigated the structural plasticity of chromatin and the role of histone H1, revealing mechanisms for dynamic regulation of 30-nm chromatin fibers. Much of his research is on histone variants. Thus, he shows that HJURP is a specific chaperone for CENP-A deposition at centromeres, critical for kinetochore organization, and that the YL1 chaperone facilitates ATP-dependent replacement of H2A with H2A.Z through structural changes in the α C helix. He demonstrated that H2A.Z is not required for transcription in postmitotic muscle cells, but prevents premature senescence by recruiting Ku80 for DNA repair. Regarding the H2A.Bbd variant, Prof. Dimitrov's group found that it forms "open" nucleosomes with 130 bp of DNA, increasing the access of transcription factors, and that SWI/SNF cannot mobilize these nucleosomes, which highlights their structural uniqueness. His research is of key importance for understanding the epigenetic regulation of various diseases. He showed that macroH2A represses transcription by blocking NF- κ B and inhibiting nucleosome remodeling by SWI/SNF. He linked epigenetic mechanisms to aging by describing disorders in H2A.Z-mediated DNA repair, which lead to mitochondrial dysfunction and accumulation of oxidative damage. These studies reveal mechanisms of histone organization, demonstrate a link between structural changes in nucleosomes and cellular functions (mitosis, repair, transcription) and refine the role of histone variants in maintaining genomic stability, opening new opportunities for studying epigenetic regulation in cancer, neurodegenerative diseases and aging. His dissertation work is undoubtedly a work carried out in scientific teams under his leadership using the most modern molecular biological and biophysical methods.

As material in the dissertation, Prof. Dimitrov presents 16 key articles on the topic in journals such as Nature, Nature Structural and Molecular Biology, PNAS, Nucleic Acid Research, etc. Professor Dimitrov has more than 120 articles on the topic since the award of his Ph.D. degree in 1982. After excluding all self-

citations, according to Scopus, his Hirsch index is 43, and his citations are 6231. His production covers and many times exceeds the criteria under the Bulgarian Law on Scientific and Technical Research of the Republic of Bulgaria for obtaining the scientific degree "Doctor of Sciences" in the professional field 4.3 Biological Sciences (Molecular Biology). In particular the citations of his articles carry 12400 points out of the required 100. Thus, this procedure aims to project into our national system of scientific degrees the recognition that Prof. Dimitrov has received in the global scientific community as the head of a team awarded as an Outstanding research group by the National League against Cancer of France, a team awarded the highest rank for exceptional scientific achievements, and other similar distinctions and awards. Undoubtedly, recognition on a different scale. Professor Dimitrov is a professor emeritus of the CNRS and has a rank of his achievements that places him in the top 3% of scientists in the field of biomedicine in France. He is currently an honorary member of the Turkish Academy of Sciences, a foreign member of the Indian Academy of Sciences. At the Bulgarian Academy of Sciences he is a foreign member, but he has also been awarded an ERA Chair in the HORIZON Europe program.

Based on these unambiguous indicators and the significant real scientific contributions of Prof. Dimitrov, I vote, and I recommend that the members of the Scientific Jury vote, with a positive vote for the award of the scientific degree "Doctor of Sciences" to Prof. Dr. Stefan Dimitrov.

Sofia

07.02.2023



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