

Final Report

COST Action CA15214

**An integrative action for multidisciplinary studies on cellular structural networks
(EuroCellNet)**

Work Group Meeting

Epigenetic Significance of Higher-Order Chromatin Structures and Their Dynamics in Norm and Pathology

June 21-22, 2018, Sofia, Bulgaria

Hosting Institution: Laboratory of Molecular Genetics, Institute of Molecular Biology “Roumen Tsanev”,
Bulgarian Academy of Sciences

Proposers:

George Miloshev (miloshev@bio21.bas.bg)

13 participants from 7 countries attended.

In his welcome address prof. George Miloshev from the Laboratory of Molecular Genetics, Institute of Molecular Biology, Bulgarian Academy of Sciences, thanked all the participants for their interest and attendance. In his talk he paid attention to the importance of COST initiatives and the opportunities they provide – for example short term scientific mobility and young scientists scholarships for laboratory visits. Prof. Miloshev stressed on the most desired outcome of the meeting – namely, inter-participant exchange of detailed information on their work and research interests. According to him the meeting would be more than successful if it turned out to be a start for future joint projects.

The participants had the opportunity briefly to introduce themselves, their career paths and current projects.

Here are short excerpts from the topics of the participant's presentations:

The talk session started with Prof. **Miloshev's** presentation on the role of linker histones in the building and maintenance of higher order chromatin structures and their role in norm and pathology. He paid special attention on the specific class of linker histones and their role in chromatin organization – main object of interest at the Laboratory of Molecular Genetics. Another point of the talk was the method Comet assay and some of its modifications, developed at the same Laboratory. He noted the variant specially designed for chromatin studies called Chromatin Comet assay (ChCA). At the end, prof. Miloshev mentioned some of the most important current research projects of his team in order to provoke discussion on possible future collaborations on interdisciplinary projects.

The topic of Prof. **Fleming's** talk was the interplay between two antagonistic chromatin remodeling complexes – the transcription co-activating Swi-Snf and the transcription co-repressing Tup1-Cyc8(Ssn6) complexes. Recent research at prof. Fleming's laboratory revealed the genes in yeast which are under regulation by these two complexes. Prof. Fleming interpret their results in the light of the site-specific chromatin organization and remodeling.

Prof. **Erenpreisa** from the Latvian Biomedicine Research and Study Centre, Riga, Latvia, raised a discussion on the dynamic nature of transcriptional regulation. Prof. Erenpreisa explained in details the design of some previous and current experiments, as well as the outcome of their work on chromatin dynamics. She presented their laboratory's results on the crucial role that heterochromatin plays in the regulation of global genome transcription.

Prof. **Sendemir-Urkmez** from Ege University, Izmir, Turkey, presented her recent work on the effect of mechanical factors on the normal function of mammalian neurons. Through their mechanical force light brain injuries may influence cytoskeletal organization, thus influencing signaling pathways and epigenetic regulation. Prof Sendemir shared information on the models and techniques which can be used for studying possible consequences of traumatic injuries on central neuron system.

Assoc. Prof. **Christina Popescu** from the Department of Experimental and Applied Biology at the Institute of Life Sciences, Vasile Goldis Western University, Arad, Romania shared her experience regarding her clinical work with prostate cancer patients. Pointing out some drawbacks of current diagnostic tests, she proposed research on the methylation status of blood cells as possible epigenetic marker for monitoring the stage of disease progression.

Prof. **Yannis Missirlis** from the University of Patras, Greece, made his colloquies acquainted with the role of mechanical signals in chromatin dynamics. He pointed out that, although mechanical signals accompany

organisms from the very beginning of their development, their role in nuclear and cellular function is still barely unknown.

Assoc. Prof. **Petar Podlesniy** from the Institute of Biomedical Investigations, Barcelona, Spain, presented a newly modified PCR technique – selfie-dPCR. Overcoming a main disadvantage of the so far known qPCR techniques, selfie-dPCR enables gene transcription quantification without using reference genes as a control. Prof. Podlesniy explained the principle of the method, and gave some implementation examples from the experimental work held in his laboratory.

Assoc. Prof. **Milena Georgieva** from the Laboratory of Molecular genetics, Bulgarian Academy of Sciences, Sofia, Bulgaria, closed the talk session of the meeting with a summary on the role of linker histones for the maintenance of the genome stability and proper genome functioning in the times of stress. She presented some of the results of Laboratory of Molecular Genetics, proving that the lack of interaction between linker histones and a key chromatin protein leads to more sensitive to stress yeast cells and definitive premature phenotypes of premature ageing.

During the Q&A sessions the participants pointed out the following questions about research results and common problems of science:

- Does the chromatin need a nuclear matrix in order to be remodeled?
- How does the chromatin structure react under mechanical stress? Can we use the term “mechanoepigenetics”?
- Are there different chromatin remodeling complexes taking part in different kind of stress responses?
- Does the chromatin remodeling induce ageing or vice versa?
- Can yeast be used as a model system when studying DNA methylation?
- How can we optimize 3D artificial cellular structures in order to grow the cells in optimal environment, closest to the natural one?
- What more can be done in optimizing the non-invasive techniques in disease monitoring and diagnosis?

During final discussion on the outcomes of the meeting and future prospects the following ideas were shared:

- Young scientists (master students and PhD students) and early career investigators should be more active in using the opportunity of short term mobility, provided by COST.
- In Romania and Bulgaria more bioinformatics specialists must be recruited for the needs of clinical research.
- Scientists have to alarm that because of the growing interest of quick translation of science into practice small research groups meet obstacles in performing fundamental research.
- Research collaboration should be implemented not only between members of one and the same COST groups, but also between different COST working groups, working on similar scientific problems.

During this meeting two important agreements have been achieved:

Dr. Podlesniy agreed to accept in his laboratory a member of Prof. Miloshev's lab for joint research on further applications of the Selfie PCR. The possibilities of the COST action CA 15214 will be used for the purpose.

Profs. Sendemir-Urkmez and Miloshev decided to prepare a grant application proposal to the Bulgarian Ministry of Science and Education on the basis of Prof. Miloshev's involvement as a MC of the COST action CA 15214. The proposal will aim studying of the mechanobiology and epigenetic properties of cells used for bioprinting.