



Latvian Biomedical
Research and Study Centre
research and education in biomedicine from genes to human



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Report on the results of the Workshop WG 1, COST ACTION Ca 15214 (EuroCellNet) in Riga, July 4-5, 2018. “ Nuclear lamins, nuclear organization and transcription”

Organizers: Jekaterina Erenpreisa (Dr.hab.med) and Latvian Biomedicine Research&Study Institute (BMC) as a host organization and venue of the conference.

Ratsupites 1k-1, Riga, LV1067

The Workshop was announced at the home page of BMC two months before the event and by personal e-mail invitations to the members of the Latvian Society for Cell Biology. The participants received the printed Program and Abstracts.

Participants – 13 scientists from abroad, 4 Latvian speakers and poster presenters – altogether 17 persons from 9 countries (Latvia, Estonia, Poland, CR, Israel, Germany, Italy, UK, USA).

Reimbursed by COST:

Prof. Yosef Gruenbaum (MC EuroCell Net, Hebrew University of Jerusalem, Israel)

Dr. Reet Kurg (MC EuroCell Net, Technological Inst., Tartu University, Estonia)

Prof. Maria Jolanta Rędownicz (Nencki Institute of Experimental Biology, Warsaw, Poland)

Participated with own funding source

Prof. Christoph Cremer (Inst. Mol Biol., Mainz, Germany); Prof. Alessandro Giuliani (Istituto Superiore di Sanità, Rome); Prof. Michael Hausmann (Kirchhoff Inst., Heidelberg University/); Prof. Harry Scherthan (Bundesw. Inst. Radiobiol with Ulm University); Prof. Igor Sharakhov (Virginia Tech., USA); Dr. Andrejs Braun (Barts Cancer Inst., UK); Dr. Martin Falk (Inst. of Biophysics CAS, Brno, Czech Rep.); Assist. Prof. Maria Sharakhova (Virginia Tech., USA); Dr. Iva Falkova (Inst. of Biophysics CAS, Brno, Czech Rep); Dr. Tetyana Klymenko (Sheffield Hallam University, UK); Dr.h.m. Jekaterina Erenpreisa (BMC, Latvia); Dr. Kristine Salmina (PhD, BMC, Latvia); Jekabs Krigerts (BsC/master student University Latvia); Dr. Talivaldis Freivalds (University of Latvia).

Attending and questioning (in addition) about 15 persons (see the attendance list) from the Latvian Cell Biology Society, professors and students of the University of Latvia, Riga Technical University, Latvian Inst of Organic Synthesis, BMC.

The Workshop was carried out according to the program, chaired by Jekaterina Erenpreisa on July 4 and Yosef Gruenbaum, on July 5.

The attendants were acquainted with the current state of art in the introductory part of lectures: on nuclear periphery and lamins (Gruenbaum); principles and current achievements of microscopic super-resolution (Cremer, Hausmann); nuclear motors (actin-dependent myosins) in transcription (Rędownicz), the thermodynamics of dissipative biological structures (Giuliani), principles of the whole genome regulation by positional information, replication timing, and rhythms (Erenpreisa); the world of nuclear RNA-methyltransferases (Kurg), biology of PML bodies (Falk), nuclear lamins in macroautophagy (Braun).

In a more specific aspect, on the first day, the influence of mechanical stress on the relationships between cytoskeleton, nuclear membranes and chromatin (Gruenbaum), the secondary and tertiary structure of the lamin-associated domains, possible participation of the centrosome-microtubule-driven epichromatin in monitoring of telomere ends and cleansing of cell nuclei from circular DNA in senescence and stress (Erenpreisa, specified in addition by the poster of K. Salmina, J. Krigerts, T. Selga, T. Freivalds, J. Erenpreisa), and the spatial influence of the chromatin-lamin attachments on the intranuclear interactions of chromosomes (Sharakhov, employing cytogenetic and Hi-C capture methodology) were presented. A. Bran and T. Klymenko presented their very recent investigations of the role of nuclear lamin for somatic hypermutation in immunity and the role of lamin impairment for development of B cell malignancy. These lectures, the questions and discussion around highlighted a leading role of lamin-chromatin interactions, genetical, structural, and biophysical, in cell nucleus organization, adaptation to stress and in cancer.

On the second day, in the first part, the results of application of the super-resolution methods (down to the single molecule level) on studies of different conditions (normal and cancer cells, ischemia) and in radiobiological experiments presented by C. Cremer, M. Hausmann, H. Scherthan and M. Falk allowed to reveal fine structural dynamics of the chromatin rearrangements in hypoxia, DNA damage and repair, in fact opening a new field of opportunities in biophysics of the chromatin. The second part was devoted to regulation of the whole nucleus organization and function, introduced by the comprehensive insight of Prof. Giuliani on the essence of the networks as dynamic dissipative structures self-organised by fluctuations, under-explored hitherto - as a perspective for future. The lecture of J. Erenpreisa on positional information of the heterochromatin, observed supra-chromosomal networks and their functional fluctuations in transcription, based on previous, some recent experimental material, and literature was a continuation of this theme. A very young researcher, Jekabs Krigerts (supervised by J. Erenpreisa and K. Salmina) presented the results of his studies by image analysis showing interrelation between spatial, quantitative and conformational change of hetero- and euchromatin in a cancer differentiation model – partly resulting from collaboration with Michael Hausmann (Germany) and Japanese biophysicists (M. Tsuchiya and K. Yoshikawa). As well, some approaches for nuclear networks studies were presented by J. Erenpreisa (partly in collaboration with Reet Kurg (Estonia)). Martin Falk presented very interesting data on the involvement of PML bodies in regulation of senescence and radiation repair. Iva Falkova showed the results of studies of the pre-malignant myelodysplastic syndrome, characterised by the genome instability as found by chromosome aberrations and cell nucleus structure change. Reet Kurg very skillfully introduced the data linking transcription, both in the nucleolus and nucleus, with translation in the world of RNA methyltransferases, thus adding the lacking functional link and revealing possibilities for collaboration of this field of research. Finally, M-J Rędowicz presented her own data on the nucleolar myosin VI connecting transcription with the elastic nuclear and cytoplasmic network, which showed many new potential targets for dynamic studies in future collaborations.

So, the main aspects of nuclear lamins, nuclear organization and transcription were presented interdisciplinary and integratively including vigorous biophysical approaches, and were discussed. Besides the existing collaboration between Erenpreisa (Latvia) and Kurg (Estonia), which was outlined for the near future decisively, it was found useful to start collaboration with M-J Rędowicz, for which first a working visit of Erenpreisa to Nencki Institute, Warsaw

will be applied. Prof. Yuri Dekhtyar (Institute of Biomedical Engineering and Nanotechnologies, Riga Technical University) is interested in collaboration with Tartu Technology Institute (presented by Dr. Reet Kurg, its director) and radiobiologists from Germany (Hausmann and Scherthan). Prof. Gruenbaum (Israel) and Dr. A. Braun (Barts University, UK) can find a mutual platform on the involvement of lamin impairment in lymphomagenesis, which should also involve the mechanobiological skeleton.

In the general final discussion, the participants expressed satisfaction with the exchange of results and opinions. The idea to choose one model of the general genome activation for cell fate change (e.g. differentiation) and to study it in the laboratories of participants applying their elaborated methods and expertise (super-resolution, life imaging, immunofluorescence, electron cytochemistry, transfection essays, transcriptome analysis, Hi-C capture, etc) testing association of the nuclear structures with ultradian rhythms and applying computer modeling was suggested. However, at present, the role of heterochromatin in such regulations is poorly understood and it seems rational first to carry out another WG1 meeting concentrating on heterochromatin, tissue-specificity and replication timing linked to lamin (possibly in Sapienza Universita di Roma, where a long-standing school of cytogenetic evolutionary studies of heterochromatin is established) in the nearest future. We also revealed lack of basic education in Systems Biology in students, which impedes further progress in basic biology and pathology, including senescence-related diseases and cancer. The future scientists should understand that living systems, including cell nucleus, are fluctuating. These fluctuations creating the functional networks cannot be carried out without the involvement of elastic microfilaments (mechanobiology).

Dissemination of Results: The participants and listeners received a certificate of participation with the COST Action and EU logo, signed by J. Erenpreisa. With permission of the author, the lecture by Prof. Alessandro Giuliani “Biological space-time: a still unexplored territory” presented as animated ppt will be installed in the videoversion in Youtube. Prof. Nikolai Sjakste (Latvian Inst. of Organic Synthesis, Riga) suggested to J. Erenpreisa (both members of the Latvian Academy of Sciences) to organize a Meeting in the Latvian Academy of Science on non-canonical DNA structures, where they can present the results from both laboratories. It would be good to organize a series of lectures with support of COST in the Universities of at least a few ITC countries, if MC members could favor this in the Universities of their countries. The lecturers could be Prof. A. Giuliani and Dr. J Erenpreisa (e.g., 4-5 lectures in two days). The lectures can be also prepared for dissemination in YouTube. It would be good to suggest this idea for discussion in the EuroCellNetwork COST Action, may be some other System biologists from the participating countries can be also revealed and involved. This additional network may in future support with ideas and modeling options the nascent one.

This report has been approved by the members of the Workshop

12.07.2018

Je. Erenpreisa