In European countries and North America, high rates of Burkitt lymphoma are found preferentially among patients infected with HIV. Interestingly, HIV is mostly associated with B cell lymphomas although it does not infect B cells. Oncogenesis in HIV infected patients may be connected with the action of a small viral protein Tat, which is able to exit infected T cells and enter other cells via its cell-penetrating domain. As Tat affects expression of host cell genes, we hypothesized that Tat protein could affect expression of B cell genes; this could trigger lymphomagenesis in HIV infected patients. To analyze the effect of HIV 1 Tat, we developed B cell lines ectopically expressing Tat protein. To discover genes that are regulated by Tat, total RNA was collected and RNA seq-based differential expression analysis was performed. We identified six KEGG pathways affected by Tat including virus response, cytokine cytokine receptor interaction pathway, ubiquitin mediated proteolysis pathway. Unexpectedly, when comparing genes modulated by Tat in B cells with those deregulated by Tat in T cells, we observed just a small overlap between the two sets. In conclusion, Tat protein appears to behave differently in B cells and T cells, exploiting distinct mechanisms to generate a specific environment in different tissues.

The work was supported by Russian science foundation (project № 17 -75- 20199).

doi: http://dx.doi.org/10.7124/bc.0009F1

N-1. Large-scale distinct H2A and H2B redistribution detected in live Jurkat cells after Doxorubicin

Péter Nánási¹, László Imre¹ and Gábor Szabó¹

¹ Department of Biophysics and Cell Biology, University of Debrecen, peternanasi@med.unideb.hu

We used confocal microscopy to detect prefixed immunfluorescently labeled histones and laser scanning cytometer to detect histone aggregation. Results: Using Confocal Microscopy (CLSM), we observed marked differences between the effect of doxorubicin (Dox), applied in a concentration range between 0.6-36 µM, on the intracellular distribution of H2A vs. H2B in Jurkat cells. Aggregation was assessed by Laser Scanning Cytometry (LSC), via the retention and consequential accumulation of histones in permeabilized nuclei of cells showing no signs of apoptosis. Aggregation was observed only in the case of H2A, while the dominant effect of the anthracyclin on H2B was the massive accumulation of the histone in the cytoplasm concomitant with its disappearance from the nuclei. The latter phenomenon was not affected by inhibitors of protein and RNA synthesis, by Tanespimycin, an hsp70 inhibitor, and by leptomycin B, a nuclear export inhibitor. On the other hand, cytoplasmic accumulation was completely diminished by PYR41, an inhibitor of ubiquitylation,
when H2B showed a H2A-like aggregated pattern in the nuclei. The cytoplasmic accumulation of H2B was confirmed also by mass spectrometric identification of elevated levels of H2B following Dox treatment in the dechromatinized samples. Conclusions: Anthracyclines are widely used anti-cancer drugs exhibiting pleiotropic effects. At the chromatin level these include topoisomerase inhibition, DNA intercalation, aggregation of chromatin, histone eviction as well as direct binding to histones. The above large-scale effects were detected already at Dox concentrations that overlap serum peak levels reached in the typical clinical setting and therefore can be a factor both in the anticarcinogenic mechanism and in the side-effects of this anthracyclin.

This work has been supported by OTKA K128770 and GINOP-2.3.2-15-2016-00044.

doi: http://dx.doi.org/10.7124/bc.0009F2

**O-1. The role of the nuclear lamina in cell migration: the connection with aging and metastasis**

N. L. Ovsiannikova\(^1\), S. V. Lavrushkina\(^3\), A. S. Yudina\(^1\), O. S. Strelkova\(^2\), O. A. Zhironkina\(^2\), I. I. Kireev\(^2,3,4\)

\(^1\) Faculty of Bioengineering and Bioinformatics, Lomonosov Moscow State University, Moscow, Russia; \(^2\) A.N. Belozersky Institute of Physical and Chemical Biology, Lomonosov Moscow State University, Moscow, Russia; \(^3\) Faculty of Biology, Lomonosov Moscow State University, Moscow, Russia; \(^4\) National Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V.I. Kulakov of Ministry of Healthcare of Russian Federation, Moscow, Russia

nat.ovs94@gmail.com

Regulation of cancer cell migration remains one of the main tasks of practical biochemistry and molecular biology. One way to solve this problem is to control the elastic properties of nucleus since it is one as the biggest and stiffer compartment that determines the cell flexibility. At the same time, the nuclear rigidity is affected by the mechanical properties of the nuclear lamina (NL), a protein meshwork underlying the inner nuclear membrane. Ratio changing of its main structural components – an A- and B-type lamins – is likely to be a key factor in the mechanical properties of nucleus. Furthermore, progerin, a mutant form lamin A, which induces Hutchinson Gilford Progeria Syndrome, is involved in aging by accumulation in NL, leading to nuclear stiffness increasing. However, how progerin presence in NL and changing of lamins ratio effect on cell migration processes is still unclear. To estimate the effect of lamins ratio changing on cell migration, we obtained HT1080 cell lines expressing GFP–lamin A, GFP–progerin and shRNA_LMNA, which specifically prevents the production of lamin A. Cell migration ability was estimated by using scratch and transwell (with 3 and 8 μm pore size) assays. The changing of NL composition is turned out to have no effect on migration in unrestricted space (scratch assay). Both overexpression of lamin A and progerin expression reduce the efficiency of cell migration through 3 μm pore size membranes. Meanwhile, the suppression of lamin A expression has no effect on migration in a transwell. Our data, especially, from scratch assay show the absence of toxic effects of