survival difference in NSCLC patients with high Post-CRT ALT (HR = 0.912, 95%CI; 0.841–0.990, $P = 0.027$).

Conclusions: There exists a clinically relevant relationship between Pre-CRT FER concentration and the prognosis of survival in patients with NSCLC. Elevated FER is the result of inflammation rather than body iron overload. Ferritin showed negative correlation with survival so it could be a useful biomarker to indicate bad prognosis of the patients with NSCLC. Additionally, CRP which is easy to detect and feasible for the use in the routine clinical practice should be considered in the prognosis of NSCLC patients.

Keywords: ferritin, nonsmall cell lung cancer, survival, C-reactive protein.

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Differences of global methylation profiles in L929 and HeLa cells treated with a serial benzoxazole and benzamide derivatives

F. Zilifdar[1], E. Foto[1], T. Ertan-Bolelli[2], I. Yalçin[2], E. Aki[2], N. Diril[1]
[1]Hacettepe University, Ankara, Turkey, [2]Ankara University, Ankara, Turkey

Epigenetic therapy tries to reverse the aberrations followed to the disruption of the balance of the epigenetic signaling ways through the use of natural and synthetic compounds, active on specific targets, such as DNA methyltransferases (DNMTs). We previously synthesized some benzoxazole and benzamide derivatives which might have anticancer activities on account of their heterocyclic structure. Our studies showed that not only these compounds caused selective cytotoxicity towards cancer cells (HeLa) with little or no toxicity on normal cells (L929) but also were not genotoxic. In this study, we aimed to test whether these compounds changed global demethylation profile of normal and cancer cells.

We used methylation specific comet assay (MSC assay) to determine global methylation levels of cells. Cells were treated with the tested compounds at IC_{50} concentrations for 48 h. Slides were prepared as did in alkaline comet assay, then they were incubated with methylation specific restriction enzymes (MspI, HpaII) before electrophoresis. Differences in global methylation levels between nontreated control cells and cells treated with compounds were compared by using tail moment data. 5-aza-C, a demethylating agent, was used as reference drug.

MSC assay results revealed that none of the tested 9 compounds caused hypermethylation on both cell lines. However, global methylation levels decreased statistically ($P < 0.05$) through both cells treated with c-2 and c-8. Only c-3 decreased methylation level on L929 but not on HeLa.

Consequently, c-2 and c-8 caused demethylation on HeLa cells similarly with 5-aza-C at low concentrations. For the reason that DNA methylation is regulated mainly DNMT enzymes in the cell, c-2 and c-8 might cause global demethylation in the cell by inhibiting DNMT activity. Further studies will be done to support this prediction.

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How immune cells can affect miRNAome and nudge the epigenetic disorganization leading to the tumour promotion

V. Halytskiy, **S. Komisarenko**
Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine, Kiev, Ukraine

Overall, macrophages and some subtypes of lymphoid cells are found in tumour stroma. These cells secrete a variety of growth factors, proinflammatory cytokines and chemokines, esp. TNF-a, IL-1b and IL-6, causing the formation of inflammatory microenvironment around tumour cells. TNF-a and IL-1b signaling increases activity of NF-kB pathway. At the same time, IL-6, triggers JAK-STAT signaling pathway, which effector is STAT3. NF-kB and STAT3 activity facilitates hyperexpression of miRNAs miR-155, miR-181 and miR-21 as well as down-regulates expression of miRNAs miR-15/16, miR-199 and let-7. This investigation aims to identify in what way these shifts in miRNAome can lead to epigenome reorganization supporting the cell transformation.

MiRNA targets within gene transcripts were predicted *in silico* using TargetScan software.

Transcripts of *HDAC2/4/8/9* and *SIRT1/5* genes encoding histone deacetylases carry targets for at least one of up-regulated miRNAs miR-155, miR-181 or miR-21. Also, these miRNAs can silence *EZH1*, *MLL*, *MLL3*, *NSD1*, *SETD6/7/8*, *SMYD1*, *SUV39H2* genes encoding histone methyltransferases. MiRNA miR-21 suppresses gene encoding *de novo* DNA methyltransferase DNMT3B. At the same time, down-regulation of miRNA miR-15/16 can allow hyperexpression of gene encoding acetyltransferase Elp3.

These shifts impair DNA and histone methylation, cause the increase of overall level of chromatin acetylation and expression and, therefore, create epigenetic background for reactivation of silent transposons, oncogenes as well as other genes important for cell transformation.

Immune system can paradoxically facilitate the tumour growth instead of healing. Cancer-related inflammation leads to the miRNAome and epigenome shifts contributing to the tumour promotion and progression.

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Discovery of BET bromodomain inhibitors with novel scaffolds and its application to treat cancers

H. Kim, A. Imran, K. Lee, **G. Choi**
Korea Research Institute of Chemical Technology, Daejeon, Korea

Lysine acetylation is one of the key mechanisms to regulate chromatin structure and transcriptional activation. Acetyl-lysine modifications are recognized by bromodomains, which are small interaction modules found on diverse proteins including histones. Among these acetyl-lysine reader proteins is the family of the BET (bromodomain and extra-terminal) proteins which contain tandem bromodomains (BD1 and BD2). The recent discovery of potent and specific inhibitors for the BET family proteins has stimulated intensive research activity in diverse therapeutic areas, especially in oncology, where BET proteins regulate the expression of key oncogenes and anti-apoptootic proteins. Several BET inhibitors are currently in clinical trials and reported to exhibit promising clinical activities. However, pleiotropic nature of BET proteins regulating tissue-specific transcription has raised safety concerns and suggested that attempts should be made for domain-specific targeting. Here, we report the recent progress in the development of BET inhibitors in Korea Research Institute of Chemical Technology (KRICT). We have identified the BET inhibitors with a novel scaffold different from the previously reported diazepine and azepine scaffolds and specific for first bromodomains (BD1s). A medicinal chemistry effort is currently made to optimize the pharmacokinetic properties of these lead compounds for further drug development. The experimental data from the biochemical and cell-based assays for these BD1-selective BET inhibitors will be presented.

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