Posters

P.YS.1

Prospects for the use of sorafenib in potential targeted pharmacotherapy of bladder cancer

Adam Kozik[1], Anna Misterka[1,2], Anna Wiśniewska[3], Marta Kaczor-Kamińska[2], Małgorzata Lasota[1,2]

[1] SSG of Targeted Therapy and Supramolecular Systems, Jagiellonian University Medical College, Cracow, Poland; [2] Chair of Medical Biochemistry, Jagiellonian University Medical College, Cracow, Poland; [3] Chair of Pharmacology, Jagiellonian University Medical College, Cracow, Poland

Adam Kozik <adam.kozik@student.uj.edu.pl>

Increased activation of receptor tyrosine kinases may be responsible for the invasion and progression of bladder cancer. For these reasons, sorafenib (a multikinase inhibitor) may play a major role in the potential targeted therapy of this cancer.

The aim of the study was to evaluate the effect of sorafenib on selected lines of bladder cancer. Cell proliferation was assessed with the MTS assay; by flow cytometry (FACS) using annexin V and propidium iodide (PI) - cell survival. A logistic model of inhibitor dose dependency was also fitted and half dose cytostatic IC50 values were determined. The effect of sorafenib on the expression of participating proteins was also determined in signal transduction.

Sorafenib exerted potent cytostatic and cytotoxic effects on bladder cells. This compound significantly inhibited the proliferation of all tested cell lines and mainly stimulated the apoptosis process in them. The effect was clearly dependent on the time and the concentration of the inhibitor. Its effect on the phosphorylation of selected signaling proteins was also found.

Sorafenib is a promising drug substance for use in potential targeted pharmacotherapy of bladder cancer.

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P.YS.2

Dimethyl sulfoxide (DMSO) as a source of interference in research related to sulfur metabolism

Marta Kaczor-Kamińska[1], Kinga Kaszuba[1], Kamil Kamiński[2], Maria Wróbel[1], Kacper Bugla[1]

[1]Jagiellonian University, Medical College, Faculty of Medicine, Chair of Medical Biochemistry, Krakow, Poland; [2]Jagiellonian University, Faculty of Chemistry, Krakow, Poland

Kacper Bugla <marta.b.kaczor@uj.edu.pl>

DMSO is widely used as the gold standard solvent in biological studies. Many researchers use it as a vehicle to deliver test molecules in cultured cells and as a component of formulations in *in vivo* experiments. Therefore, it is important, to be aware that the use of DMSO as a solvent may provide an additional source of sulfur and oxygen atoms or monocarbon units for various processes normally occurring in the cells. However, these side-effects are often neglected. Hence, the aim of the study was to investigate whether the addition of DMSO to the culture medium (even in amounts generally considered acceptable) alters some parameters of sulfur metabolism (i.a. activity and expression of thiosulfate sulfurtransferase (TST, EC:2.8.1.1), 3-mercaptopyruvate sulfurtransferase (MPST, EC:2.8.1.2) and cystathionine γ-lyase (CTH, EC:4.4.1.1); the sulfane sulfur-containing compounds and non-protein thiols levels). Since, the negative effects of DMSO on the cell membrane are well known, in order to eliminate these potentially destructive effects, additional experiments were carried out with partially loading of DMSO into polymerosomes (poly(ethylene glycol) methyl ether-block-poly(lactide-co-glycolide), PEG-PLGA). The results obtained indicate that DMSO is a source of interference in studies related to sulfur metabolism, and there are not just simple effects that can be corrected in the final result by subtracting the value of the control, but there are also observed complex synergisms.

P.YS.3

Myosin VI expression profile in mouse epididymal epithelium

Anna Richert[1], Piotr Wasąg[1], Robert Lenartowski[1], Anna Suwińska[1], Joanna Suszyńska-Zajczyk[2], Marta Lenartowska[1]

[1]Department of Cellular and Molecular Biology, Nicolaus Copernicus University in Toruń, Poland; [2] Department of Biochemistry and Biotechnology, Poznan University of Life Sciences, Poland
Anna Natalia Richert <503436@doktorant.umk.pl>

The epididymis is a twisted tubule divided into several segments that create distinct luminal environments for sperm maturation/storage. The epididymal epithelial cells have different roles depending on their location in the epididymis and most of them form numerous microvilli in the apical zone. Myosin VI (M6) is a unique actin-based motor involved in the structural integrity and function of several specialized epithelia in mammals, such as the intestinal microvilli epithelium, the proximal rental tubule epithelium, or the cochlear sensory epithelium. This protein is essential for normal stereocilia architecture in the inner ear, and loss of M6 function causes deafness in mice and humans. The role of M6 in the apical domain of polarized epithelial cells is related to endocytosis and anchoring of the cell membrane to the base of microvilli. To date, there are no data available on the involvement of M6 in the functional organization of the epididymal epithelium. We have recently determined that M6 depletion in Snell's waltzer mice causes structural disruptions during spermiogenesis and reduced male fertility, which may be also the result of impaired sperm maturation in the epididymis. Here, we show for the first time the expression profile of M6 in specific epididymal segments and epithelial cells using Snell's waltzer and control mice and discuss the role of M6 in this highly specialized epithelium.

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P.YS.4

Imatinib mesylate (STI-571) and its complex with Congo red in regulation of growth, survival and migration of bladder cancer

Anna Misterka[1,2], Anna Wiśniewska[3], Małgorzata Lasota[1,2]

[1]Chair of Medical Biochemistry, Jagiellonian University Medical College, Cracow, Poland; [2]SSG of Targeted Therapy and Supramolecular Systems, Jagiellonian University Medical College, Cracow, Poland; [3]Chair of Pharmacology, Jagiellonian University Medical College, Cracow, Poland
Anna Misterka <malgorzata.lasota@uj.edu.pl>

Bladder cancer is the second most frequently diagnosed cancer of the genitourinary system in Europe. Research shows that increased activation of receptor tyrosine kinases, including the PDGFR, c-KIT receptor, EGFR or VEGFR and the intracellular PI3K/AKT/mTOR pathway may play a huge role in the development of bladder cancer. The aim of this study was to determine the influence of an inhibitor of the receptor tyrosine kinase (imatinib) and its combination with Congo red on the growth, survival, and migration of bladder cancer cell lines (RT4, T24) with different malignant potential.

Exposed bladder cancer cells to the investigated inhibitors triggered a dose-dependent suppression of proliferation compared to the control. The FACS analysis showed that an inhibitor induced apoptosis of bladder cancer cells. The percentage of apoptotic cells was increased depending on the dose by inhibitor therapy. A wound healing/scratch test showed a significant decrease in cell movement after exposure to the inhibitor and its Congo red complex.

Tyrosine kinase inhibitors, such as imatinib and their combination with Congo red are a promising class of treatments for bladder cancer.

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P.YS.5

The role of GDF11 in the gastrointestinal tract

Weronika Machelak, Emilia Januszkiewicz, Mikołaj Mierzejewski, Wojciech Król, Marta Zielińska

Department of Biochemistry, Faculty of Medicine, Medical University of Lodz, Poland
Weronika Marta Machelak <weronika.machelak@stud.umed.lodz.pl>

GDF11 (growth differentiation factor 11) is known for its rejuvenating properties. This novel member of TGF-β (transforming growth factor β) superfamily is a key regulator of skeletal axis formation, embryogenesis, and tissue maturation. Current scientific data confirm the importance of GDF11 in pathogenesis of inflammation, fibrosis, and cancer progression. GDF11 is also considering as prognostic biomarker of colorectal cancer patients' lifespan. In our study we determined the expression of GDF11 in the gastrointestinal (GI) tract. We used healthy mice (C57BL/6) at the different age (6, 12, 18 months old) to collect tissue from different parts of the GI tract. Then, we induced the intestinal inflammation by dextran sodium sulfate (DSS), and colitis- associated colorectal cancer by DSS and azoxymethane. We collected mice tissue at different stages of inflammation and colorectal cancer for molecular analysis of GDF11 expression at mRNA (RT- PCR) and protein (western blot) level. We found that GDF11 expression level differed due to the course of experimental colitis and colitis- associated colorectal cancer in mice. Next, we evaluated anti-inflammatory action of GDF11 in experimental colitis. We presume that GDF11 affects the expression of inflammatory cytokines and positively impacts colon damage confirmed with histology assessment. The role of GDF11 in the GI tract seems to be significant in the context of the colonic inflammation and carcinogenesis.