POSTERS – RESEARCH

Cancer and ageing

P-01.1-01
Characterization of non-covalent complexes of cationic porphyrins and folic acid for photodynamic therapy of tumors

L. Mkrtchyan[1], A. Zakoyan[1], T. Seferyan[1], M. Parkhats[2], G. Gyulkhandanyan[1]
[1]*Institute of Biochemistry of the National Academy of Sciences of Republic of Armenia (NAS RA), Yerevan, Armenia,* [2]*B.I. Stepanov Institute of Physics NAS of Belarus, Minsk, Belarus*

Photodynamic therapy (PDT) involves the activation of a photosensitizer (PS) by light in the presence of oxygen and the subsequent generation of reactive oxygen species that kills cancer cells. Targeted PDT can be achieved by binding of PS with folic acid (FA) as its receptor overexpressed in cancers of epithelial origin (100–300 times higher than on healthy cells) [1]. We obtain non-covalent complexes of PSs (with cationic TOEt4PyP, Zn-TOEt4-PyP, and anionic PS 'Photosens') with FA to obtain targeted PDT. Complexes were characterized by absorption and fluorescent spectroscopy. Stable complexes were gained in presence of 20% glycerol, which improves the photostability [2]. Photobleaching of obtained compounds was decreased by L-histidine and D-mannitol as famous quenchers of singlet oxygen and hydroxyl radicals, respectively. Both quenchers had a protective effect after 30 minutes of illumination by a tungsten lamp, therefore both singlet oxygen and hydroxyl radicals contributed to the photobleaching [3]. Free PSs and PSs in complexes with FA had similar spectral changes when the concentration of sodium chloride (0–0.9%) and pH of the medium (7–6.2) changed. Therefore these changes are characteristics of PSs themselves. To evaluate the effectiveness of lipid peroxidation by PSs and their complexes, a liposomal model was used, and the oxidation was monitored by thiobarbituric acid test for detection of MDA (malondialdehyde). All tested PSs and their complexes with FA led to the production of MDA as the secondary product of lipid peroxidation, following illumination. The complexation of PSs with FA, led to no changes in singlet oxygen quantum yield, which suggest their effectiveness for PDT. Funding: Grant SC RA No 21SC-BRFFR-1F007 1. Fernández M et al. (2018). Chemical Science 9 (4), 790–810. 2. Previously published in: Mkrtchyan L.V. (2022) Biolog. Journal of Armenia 74 (1), 31–38. 3. Previously published in: Mkrtchyan L.V. et al. (2022) Proceedings of SUSTENG 2022, 518–523.

P-01.1-02
Alternative routes for HB-EGF mitogenic effects inhibition

A. Siromolot[1,2], D. Kolybo[1]
[1]*Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine, Kyiv, Ukraine,* [2]*Taras Shevchenko National University of Kyiv, Kyiv, Ukraine*

Heparin-binding epidermal growth factor–like growth factor (HB-EGF) is a member of the epidermal growth factor family and has a variety of physiological and pathophysiological functions. Also, HB-EGF plays a pivotal role in distinct tumors progression. HB-EGF is highly expressed in certain cancer cells, such as ovarian and breast cancers, that makes it beneficial for the development of antitumor therapeutic agents. Neutralizing agents against HB-EGF can act on two strategies: sterically blocking the binding of HB-EGF with receptors (monoclonal or polyclonal antibodies, diphtheria toxin derivatives) or capable preventing the formation of soluble HB-EGF from proHB-EGF (ectodomain shedding) with MMPs or ADAMs inhibitors. Recombinant analogs of *Corynebacterium diphtheriae* toxin fragments (subunit B) and it toxoid CRM197 are able to block the binding of fluorescent derivative HB-EGF (HB-EGF-mCherry) with receptors HER1 and HER4 on the surface of *A431* and *Vero* cell lines. It has been shown that immune serum-containing polyclonal antibodies against HB-EGF is able to inhibit HB-EGF binding to surface cellular receptors and block the mitogenic activation with HB-EGF of cells by deactivating Ras-MAPK/ERK1/2. Mitogenic activity of sHB-EGF is significantly enhanced by membrane-associated heparan sulfate proteoglycans (HSPG). Interaction of the N-terminal heparin-binding region of HB-EGF with HSPG leads to stabilization of the EGF-like domain of the molecule in complex with the receptor. The ability of heparin to block proliferation of A431 and Vero cells by exogenous HB-EGF has been demonstrated, probably, due to binding with heparin-binding domain of HB-EGF. Moreover, leupeptin and a broad-spectrum metalloproteinase blocker GM6001, and EDTA significantly decrease paracrine activation of cells by HB-EGF. Thus, searching and development of effective neutralizing agents against sHB-EGF is important and perspective research direction for establishing of a new targeted antitumor therapy.

P-01.1-03
Effects of NRF2 inhibition on chemosensitivity and gene expression in KRAS mutant colorectal cancer cells

C. Geyik[1], J.C. Namli[2], B.M. Açar[2]
[1]*Department of Medical Biochemistry, Faculty of Medicine, Istinye University, Istanbul, Türkiye,* [2]*Istinye University, Istanbul, Türkiye*

Colorectal cancer (CRC) is highly metastatic and dangerous among cancer types with high mortality rate. Treatment options usually suffer from individual genetic differences affecting drug metabolism and bioavailability. Mutation in KRAS gene has detrimental consequences in CRC. One of the effects of these mutations is activation of NRF2, a transcription factor that regulates several important metabolic pathways including redox homeostasis, xenobiotic metabolism, and biosynthesis. Inhibition of NRF2 seems a promising strategy to overcome some of the problems in CRC therapy. In this study, NRF2 is inhibited by a small molecule inhibitor, ML385, in two CRC cell lines: HCT 116 (KRAS mutant) and HT-29 (KRAS wild-type). Effects of this inhibition on irinotecan chemosensitivity was determined by co-administration of these drugs in SRB cell viability assays. Several targets of NRF2 were compared after ML385 administration in both cell lines to determine the differential effects in KRAS mutation. 2-step RT-qPCR was used to compare NRF2 targets and GAPDH was used as housekeeping gene. ML385 alone slightly decreased cell viability but there was no significant