abstracts: poster presentations

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MYC-nick. Unexpectedly, we found that MYC-nick promotes an increase in purines. Utilizing HPLC-Mass spectrometry (in collaboration with Dr. Noelle Williams), we found that MYC-nick expression induces purines in fibroblasts and in human colorectal cancer cells. Moreover, we also found that purines are elevated in human colon cancer tissues, which express high levels of MYC-nick. The most dramatic result was an increase in the levels of deoxyinosine (a mutagenic purine) in every tested biopsy sample of colon cancer.
We propose that MYC-nick increases the production of purines by shunting glycolytic intermediates into the pentose phosphate pathway to promote de novo purine synthesis. We hypothesize that MYC-nick, by acetylating and regulating the activity of glycolytic enzymes (such as aldolase), promotes synthesis of purines in a transcription-independent manner. Currently, we are testing the role of deoxyinosine and other purines on MYC-nick-induced cell survival and mutagenesis.

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Alpha1-antitrypsin-derived C-terminal peptide is a potent oxidative stress inhibitor.

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Acute-phase protein alpha1-antitrypsin (AAT) has been reported as a biomarker in many tumors. A number of tumor cell lines produce the protein. Tumor-associated proteases cleave AAT at the active site producing a bioactive C-terminal peptide C36, which possesses immune suppressing, serine protease-protecting and mitogenic activity (L. Cercek, B. Cercek, 1992, 1993; Zelvyte I. et al., 2003). According to our previously reported data, C36 can also activate metabolism under certain conditions (Maslakova A., 2016). Recently, an exogenous full-length AAT has been established as an oxidative stress protector in a human placental cell line (Feng Y-L et al., 2016, 2017) at the effective concentration of 50uM. We investigated the oxidative stress-protecting activity of AAT-derived C36 peptide in human cell line DU145 under serum starvation condition using cell-permeable 2',7'-dichlorodihydrofluorescein diacetate. We used a wider C36 peptide concentration range (10pM-50uM) in order to investigate its potential activity at levels that are much lower than physiological levels for the full-length AAT (around 30uM), that might be closer to true peptide concentrations in tumor microenvironment. Indeed, C36 peptide protects cells from oxidation in a dose-dependent manner starting from as low as 100nM (≈34% lower overall oxidation level), while 30-50uM gives a more pronounced effect (≈49-56% lower overall oxidation level, respectively). The latter inhibitory level is in a good accordance with the previous data on the full-length protein (Feng Y-L et al., 2016), that has been shown to inhibit p38MAPK signaling pathway (Feng Y-L et al., 2017). Our findings indicate that AAT-derived C36 peptide preserves the site crucial for such activity and can potently protect tumor cell from oxidative stress under serum starvation. The study was supported by RFBR project № 16-34-01095 mol_a ("Structural and functional analysis of SERPINA1 gene transcripts and alpha1-antitrypsin protein isoforms in human tumors cultured cell lines").