frequent in the TS group compared with TR group ($p = 0.043$). A significant association between *IVS7+24G>A* SNP and high TGF-βR1 protein expression was observed ($p = 0.044$). Nonetheless, among all studied polymorphisms only *ESR12014G>A* SNP was correlated with a heterogeneous distribution of ERα expression ($r = 0.353$, $p = 0.016$).

Conclusion: These data suggest that the distribution pattern of ERα expression, EGFR expression and *ESR1* 2014G>A genetic variation could be useful additional prognostic markers for hormone receptor-positive breast cancer patients treated with adjuvant tamoxifen.

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T125

Effect of carcinoembryonic antigen production by colorectal cancer cells on tumor microenvironment and cancer progression

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Tumor markers play an important role in the identification of human malignancies. It has been shown that the carcinoembryonic antigen (CEA, CEACAM5) is a promoter of metastasis in epithelial cancers that is widely used as a clinical marker. The aim of this study is to elucidate the network of genes that are involved in the CEA-induced liver metastasis. Previously, we have shown that CEA is accumulated in the lungs and livers of rats by interacting with their macrophages. We identified and cloned a new gene (CEAR) for the CEA-binding protein, which is located on the surface of fixed liver macrophages, Kupffer cells (Bajenova et al, 2001). It has been shown that the interaction of CEA and CEAR proteins increases the production of IL-1, IL-10, IL-6, TNF-α cytokines (Thomas et al, 2011). This interaction changes the expression of liver adhesion molecules that enhances the survival of cancer cells to the liver. We also suggested that CEA synthesis by cancer cells may influence the E-cadherin adhesion junction complexes and have shown that CEA production violates the functional relationship between Ecadherin and its partners α-, β- and p120 catenin. A new type of interaction was discovered between the CEA and β-catenin and the increased amount of β-catenin in the nuclei of CEA producing cells. The data show that CEA production can cause the dissociation of cancer cells and trigger cancer progression. The CEA synthesis also alters splicing of p120 catenin protein and causes the release of soluble E-cadherin. Previously, CEA and epithelial E-cadherin were considered as independent tumor markers. Our data explain the correlation between the elevated levels of CEA and the increase in soluble E-cadherin in the progression of colorectal cancer (Bajenova et al, 2014).

We carried out a comparative transcriptome analysis of CEA-producing cell lines. The RNA transcriptome libraries were obtained and sequenced. By pairwise comparisons of CEA producing and non-producing cell lines using Cummerband program, we selected the set of genes (90 total genes) whose expression have been changed in the CEA-producing cell lines (overexpressed or downregulated). The biological processes that are linked to this differential gene expression were identified by Gene Set Enrichment Analysis (GSEA). In total, 8 significantly enriched GO terms related to the cellular components and biological processes were identified. Using KEGG and GO databases, we also identified the signaling pathways involved in the response to CEA. These findings have direct medical application, since they allow not only to establish the relationships between the existing biomarkers but also to discover the new ones. These biomarkers can be used for diagnosis and monitoring of metastatic carcinomas and for the drug development.

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T86

New approaches to the rational design of anticancer drugs

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Discovery of new pharmacologically active small molecules is an important and rapidly expanding area of modern molecular pharmacology. Given a limited number of proteins that are druggable, it is important to identify as many chemical effectors as possible to define the best regimen of anti-cancer therapy in each particular case. An E3 ubiquitin ligase, Mdm2, which mediates ubiquitin-dependent degradation of the critical tumor suppressor p53, is a promising target for small molecule inhibitors. Using a hybrid approach which combines the rational design of small molecules selected from the virtual library and the high-content screening using cancer cell lines we discovered several new inhibitors of the p53-Mdm2 interaction. These compounds were able to activate and stabilize the p53 protein causing massive apoptosis preferably in p53-positive cells at rates higher than the well-known inhibitor of Mdm2, Nutlin-3. The molecular mechanisms of their action will be discussed.

As another example of rational design of potential anti-cancer drugs, we will talk about artificial nano-Matrix-Imprinted - Polymers (MIPs) that recognize the structure of peptides and other biological molecules and thus dubbed as "plastic antibodies". We have generated such nanoparticles against the surface region of the oncogenic receptor, EGFR, which is overexpressed in many forms of solid tumors. Selection of the linear epitope for creating "plastic antibodies" against the receptor was performed by analysis of a three-dimensional structure of the protein. The obtained "plastic antibodies" were specific against the epitope of EGFR. These plastic antibodies when loaded with a genotoxic drug, doxorubicin, were able to specifically induce cell death of breast cancer cell lines that overexpress the EGFR receptor. Experiments in vivo using xenografts of breast cancer cell lines pre-incubated with these plastic antibodies in nude mice showed that they have a pronounced therapeutic effect. Furthermore, since the commercial drug, Cetuximab, recognizes an epitope of EGFR, different from the one recognized by our plastic antibodies, it is likely that the latter may increase the efficacy of